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INSULIN SHOCK TREATMENT OF SCHIZOPHRENIC PATIENTS

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Our object in this paper is to record the course of Sakel's insulin treatment in individual cases—the reactions observed after the injections of insulin and the therapeutic results obtained.

In the last six months, beginning on July 20, 1936, fifteen patients received the treatment, which was carried out according to Sakel's procedure as to its essentials.[1] The treatment of ten patients was completed in January 1937. For economy of space and for the sake of presenting a fairly detailed description of our observations, this study is limited to six cases.

REPORT OF CASES

CASE 1.—H. A., aged 25, who was admitted to the Spring Grove State Hospital on April 3, 1936, had become ill about three months before, when he was found wandering about in the snow in Pennsylvania. After a month in a hospital in

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Pennsylvania he was taken home. There he said that he was dying and refused to eat; he claimed that one side of his body was cold and the other "nice and warm." His head felt "funny"; he thought he had been doped by the physicians in the Pennsylvania hospital, that they had "fixed" him with "dope." He began to smoke incessantly, although he had never smoked before. He heard voices saying, "He is going crazy." The night before his admission to the hospital he cut his wrists, saying he would rather be dead.

In the hospital, he looked preoccupied, mumbled to himself and laughed without apparent cause. "Sometimes it sounds like somebody was hollering, 'You will die of a heart attack,' but I never saw anybody there." Judgment on formal testing was poor. He missed the Binet absurdities. He realized that there was something wrong with his mind.

Physically, he was undernourished and of asthenic habitus.

The patient passed the fifth grade in school and did well. After school he worked as a cook in a bakery and as an orderly in a hospital. He was described as lively, "full of fun," of good disposition, happy and ambitious.

Outstanding Features.—These were: delusions of being doped; auditory hallucinations; peculiar somatic sensations; age 25 years, and duration of illness, seven months.

Insulin Treatment.—The total period of treatment was one month. On the first day the patient received 30 units in the morning, before breakfast; on the next five days he received 30 units in the morning and 30 units in the afternoon. Four hours after the first injection a regular meal was given; two hours later the second injection was given, followed by a regular meal after three hours.

The reactions following the injections immediately or within two hours and lasting a few hours were: restlessness; slight perspiration; talkativeness, with a euphoric tinge; singing, and moderate laughing. The pulse rate varied from 66 to 98.

On the next four days the patient received from 80 to 95 units, divided into two doses—one dose in the morning and the other in the early afternoon. The reactions as observed were: quietness; talkativeness; euphoric states, and drowsiness, confusion, mumbling and talking to voices. After the effect of insulin was counteracted by a meal, he took an interest in other patients and tried to help them with their meals. The pulse rate fluctuated from 76 to 112.

During the next twenty-one days, the patient received treatments at intervals of three, four, five and eight days—in all, six injections of 80 units each. On the first day he was quiet and dozed within two hours and thirty minutes after the injection. Then he jumped out of bed, threw himself on the floor and fought violently with the attendants, screaming: "Mother!" "Miss Ulmer!" Such outbursts were repeated during about two hours. Then he became cheerful and pleasant, talking, laughing and walking around; he had complete amnesia for the outbursts.

During the next two days, without insulin, he remained quiet, pleasant and cheerful; there was no talk of fears or voices.

After the second injection he perspired moderately for an hour. Two hours after the injection he became restless and confused, talked irrationally and perspired profusely. There was marked hyperreflexia. The pulse rate varied from 70 to 104. The respiratory rate was between 18 and 24. After he had remained one hour in this condition, he was given dextrose by mouth and a regular meal. About half an hour after that he was pleasant, said that he did not remember anything of his reaction and asked if he had carried on as he did before.

One hour after the third injection the patient complained of numbness of the feet, which progressed upward. About two hours after the injection there were profuse perspiration, extreme restlessness, screaming and "talking out of head." He fell out of bed and struck his head on the floor. After he had remained in this condition of motor restlessness for about an hour and thirty minutes, dextrose was given intravenously and by mouth. This was followed immediately by complete relaxation and spontaneous, relevant conversation. He tried to help other patients. He said that he no longer paid attention to voices because the doctors told him that there was no one about him speaking to him. On the next day he was pleasant, talking and laughing cheerfully.

The fourth injection was followed by quietness and slight perspiration for about two hours. Three hours after the injection the patient became restless, fell from bed and sustained a cut over the left eye. After he had remained in this excited state for forty minutes, dextrose was given intravenously. He complained of headache and worried about the abrasion over the eye.

During the following four days, without insulin, the patient was brighter than usual; he was pleasant and in good mood, taking care of other patients and trying to persuade the mute to undergo the insulin treatment.

After the fifth injection the patient was only slightly restless; he slept frequently and perspired moderately. Three hours after the injection he became very restless, crying, "Oh, my God!" One hour later he was asleep, and dextrose was given intravenously. When aroused, he said that he wanted to sleep.

The next seven days, without insulin, he spent in conversing with attendants, showing much interest in other patients and reading a great deal. He frequently complained of "feeling badly" in the chest and stomach and of "scares" going through him.

The sixth injection was followed by slight perspiration and slight restlessness. The reactions after this injection were the mildest. The patient had a regular meal five hours after the injection. He showed marked improvement after this injection. He then worked in the ward, taking good care of patients, and was always pleasant and cheerful and much pleased with the daily ground parole.

In spite of the pronounced reactions following the injections, the level of blood sugar remained relatively high, the lowest being 49 mg. per hundred cubic centimeters and the highest 63 mg. There also appears to have been a disproportion between the therapeutic effects and the moderate hypoglycemia.

The changes in the nonprotein nitrogen content of the blood were insignificant. The lactic acid in the blood increased after the injections. This was probably due to the motor restlessness.

The patient had his last treatment on August 12. For about three months afterward he worked in the ward and showed no abnormal behavior. At an interview with the physician he stated: "I don't smell things; I don't see things; my mind is clear; I try to keep it occupied, to forget my troubles." He wanted to go home and return to work as attendant in a hospital. On formal mental examination, he showed good judgment and grasped all the Binet absurdities in contrast to the findings before treatment.

Weight: Before treatment, on July 22, he weighed 126½ pounds (57.4 Kg.), and after treatment, on November 25, 144¾ pounds (65.6 Kg.).

Subsequent Course.—The remission, as described, lasted nearly three months. Then, gradually a marked change in behavior took place. He did not speak of hearing voices but complained continuously of all sorts of diseases, making up names for them, such as "brainitis," "blooditis," "cheesitis" and "breaditis." On December 1 he said: "I have all kinds of phobias." He has a "phobia" about

going outside and a "phobia" about work. According to the nurses and attendants, he uses these "phobias" and the fabricated names of diseases as an excuse for not doing what he does not want to do or for getting attention. Up to the time of writing (Jan. 26, 1937), the patient has remained disturbed and much concerned about his body; he is profane and vulgar, uncooperative and belligerent.

The points of interest in this case are:

1. Good therapeutic results obtained with treatment of only one month's duration.

2. Disproportion between pronounced reactions, particularly motor restlessness, and moderately low levels of the blood sugar—about 50 mg. per hundred cubic centimeters.

3. Discrepancy between good therapeutic results and moderate hypoglycemia.

4. Moderate hypoglycemia provoked by relatively high doses of insulin.

5. Relapse after a remission of nearly three months.

Case 2.—Z. R., a married man aged 28, was committed to the Spring Grove State Hospital on June 18, 1936, after a week in a general hospital and three months in St. Elizabeths Hospital, Washington, D. C. Early in February 1936 he looked "nervous and upset" and told his wife that somebody was after him. On admission to the general hospital he was agitated and depressed. He heard voices giving him conflicting directions and calling him bad names. He was "the object of persecution by communists and his fellow-workers in the bakery." In the Spring Grove Hospital he complained: "These voices—they thought I was rich and getting along; they say I am no good, that I am drunk; they are after me all the time." . . . "They want to keep me here to trap you people." The patient realized that he had "some mental trouble," that the voices were "imaginary" but that he was unable to forget them. He was undernourished and of asthenic habitus. There was muscular atrophy of the upper and lower extremities on the left—residual from poliomyelitis in early life.

In September 1936 he wrote to his wife that he thought she was running around with other men and that he would kill her the first chance he had.

Outstanding Features.—These were: ideas of being persecuted by communists; hearing voices which gave him conflicting directions and called him bad names; age, 28 years, and duration of illness, six months.

Insulin Treatment.—Insulin shock treatment was administered from September 9 to November 20; the shock dose was 65 units. From the beginning of the treatment, with a dose of 25 units, the patient was restless and complained of weakness. Motor restlessness was prominent throughout the treatment. Other features frequently observed were: talking aloud; shouting, apparently in good spirits; perspiration; transitory rigidity and quivering of the body; marked salivation and accumulation of mucus in the throat, and difficulty in breathing. On one occasion clonic convulsive movements were observed, and the shock was immediately terminated by intravenous injection of dextrose. In most treatments the shock was terminated when the patient was in a comatose state or deep coma. After the treatments and on rest days, without insulin, the patient was in good spirits, cheerful and cooperative and made himself useful in helping with the routine work

of the ward. However, he frequently complained of headache, dizziness and pains in one part of the body or another. There were doubts about these complaints because of his outspoken antagonism toward the treatment from the beginning to the end.

The level of the blood sugar during fasting remained about 80 mg. per hundred cubic centimeters. Values for the hypoglycemia varied from 22 to 50 mg. per hundred cubic centimeters. The convulsive movements were associated with a blood sugar level of 22 mg. per hundred cubic centimeters. Other marked reactions also accompanied the low sugar content of the blood, but there was no consistent relationship; nor was there a consistent parallelism between the dose of insulin and the degree of hypoglycemia.

Course.—The condition before, during and after treatment, as noted by the attending personnel, was as follows:

Before Treatment: The patient was stubborn and had to be driven to do any given task. He even refused to go out for walks and had to be dragged outside. Then he walked around with the group, but was sulky. He told other patients not to work and not to help in the ward. He wanted to lie on the bench or sit and read the whole day. He complained constantly of pain. If asked to do anything, he answered: "I am not supposed to work, because I am sick." There was no peculiar behavior. He ate and slept well.

During and After Treatment: He did not want to take the treatments, claiming they would not do him any good. Several times he had to be forced to take them. During the shocks he was noisy and combative. When the shock was terminated he wanted to sleep and refused to eat, in contrast to other patients taking insulin, who asked for food. He was always stiff and sore "because of the fighting during the shock." His condition improved after each shock. He became more responsive. When asked to work he seemed to be more willing to do so. Since undergoing the treatment (from September 9 to November 20) he has done anything he has been requested to do without protest and often asks if that is all there is to be done. There is no need to push him or even to tell him what is to be done. He has been doing his work spontaneously. He and Mr. G. (another patient receiving insulin treatment) have been shaving patients, cleaning floors, giving baths and folding bed linen. He has been much more pleasant than before.

Weight: Before treatment, on September 9 and 11, he weighed 117 pounds (53.1 Kg.), and on November 25, 131 pounds (59.4 Kg.).

Patient's Statement: "I think it helped me a whole lot. It quieted my nerves. I take life pleasanter; I keep my mind occupied by work all the time. I do it willingly; before, I didn't want to work; I felt lazy and sluggish."

Physician's Statement: "Before treatment the patient was not as cheerful, cooperative or industrious as after. He has more insight into his condition and has relinquished the ideas about his wife. Before treatment he had delusions of persecution and was resentful toward his wife and family. All this has disappeared. The family recognizes that he is greatly improved."

The noteworthy points in this case are:

1. Distinct therapeutic benefit was obtained from the treatment.

2. The convulsive movements were associated with a blood sugar content of 22 mg. per hundred cubic centimeters.

3. There was, however, no consistent relationship between the pronounced clinical reactions and the marked hypoglycemia, nor was there a consistent parallelism between the dose of insulin and the degree of hypoglycemia.

CASE 3.—J. F., aged 16, a Catholic, who was committed to the Spring Grove State Hospital on April 13, 1936, had since April 7, 1936, been seeing men dressed in black who were going to "get" him. He crawled under his bed to pull them out and called to members of his family for help. He complained that he was "ruptured" and that the umbilicus hurt. In the hospital he sat in one place, staring the whole day and soiling constantly. At times he answered questions of physicians slowly, after they were repeated to him several times, but remained practically mute after admission. He grimaced frequently and refused to take his clothes off for physical examination. Sleep and intake of food were satisfactory, although at times he had to be urged to eat. The patient had learned well in school and had left at the seventh grade. He liked farm work and had been gardening for his father and occasionally helping his brother in the store.

He was described as sensitive and touchy throughout early life, easily upset but not cranky, quick tempered and backward with strange people. He had masturbated frequently during the past year. Physical examination did not reveal any abnormalities.

Outstanding Features.—These were: delusions of persecution and visual hallucinations; mutism; grimacing; uncooperativeness, resistiveness and negativism and duration of illness of approximately four months.

Insulin Treatment.—The patient's condition was unchanged at the beginning of treatment, on July 21. For six days he received 30 units twice a day; the first dose was given early in the morning, followed by a regular meal four hours after the injection, and the second dose, two hours later. Nothing unusual was noted, either in the patient's conduct or in the physiologic reactions, except moderate perspiration and an irregular pulse, of good quality, on one occasion only. The pulse rate varied within the extreme limits of 61 and 104 but fluctuated for the most part between 65 and 80. The respiratory rate varied from 18 to 22.

On the subsequent four days from 75 to 90 units a day, also divided into two doses, was given. On two occasions he perspired profusely, and on one occasion, namely, the fourth day, he was markedly restless; after the effect of insulin had disappeared he looked brighter than usual. The lowest pulse rate was 58 and the highest 106, but most of the time the variations remained within much narrower limits. The respiratory rate varied from 18 to 22.

For the next two months the patient was given 80 units in single doses about every third day. The following reactions were observed during these treatments: perspiration and salivation, from slight to profuse; drowsiness, amounting sometimes to semistupor or a markedly stuporous state; motor restlessness, always moderate; dilatation of the pupils, and blushing and flushing of the face. The lowest pulse rate was 46, and the highest, 124; these extremes were observed only once; mostly the pulse rate varied from 60 to 90; irregularity but good quality of pulse, dilatation of the pupils and hyperreflexia were noted several times. Each of these reactions was more or less prominent in individual treatments, usually became conspicuous approximately two hours after the injection and lasted, to a more or less pronounced degree, for from two to four hours, until the effect of insulin was counteracted by the administration of dextrose, either intravenously (15 cc. of a 33 per cent solution) or by mouth (200 cc. of a concentrated solution) or by both methods.

Course.—In addition to the drowsy, semicomatose state mentioned, changes in the personality reactions were observed immediately subsequent to the treatment. These changes were: greater interest in what was going on in the ward; better rapport with the physician, attendants and patients, and more marked activity in the ward and on the lawn with other patients. Most often, after administration of dextrose the patient answered questions or talked somewhat spontaneously: "My feet hurt." (Where?) "Between my toes." Then he responded to questions only by nodding his head. During another treatment, when asked "What are you doing?" he answered, "I am in a dream world." Frequently, after the treatments he carried on a conversation or talked disconnectedly for ten minutes or more; then he again became mute, although remaining in rapport with the interlocutor. In the interval between treatments he impressed those around him as being brighter and taking greater interest in the environment, but he remained mute. Only occasionally he answered questions and read aloud a few paragraphs when repeatedly asked to do so.

During October the patient received 90 units in one dose every other day, except once, at an interval of three days, and once, at an interval of four days. The physiologic and personality reactions previously described were essentially the same during, immediately after and between the treatments. Only the respiratory rate varied within wider limits, from 16 to 28; the breathing was noted to be heavy on several occasions, and the pulse was more frequently irregular than during the previous treatment.

From November 5 to November 10 the patient received four treatments. The reactions were the same as those in the treatments last described. The level of the blood sugar during fasting, which was 90 mg. per hundred cubic centimeters before the first injection of 40 units, fell to 57 mg. four hours after the injection. During the other treatments, with 80 or 90 units, the normal level during fasting fell to as low as 44, 38 and 20 mg. per hundred cubic centimeters within from two to seven hours after the injection. In most treatments, however, the level of the blood sugar remained between 40 and 50 mg. While the most pronounced physiologic and favorable personality reactions were observed with the lowest levels of the blood sugar, similar reactions were also noted when the blood sugar remained around 50 mg. per hundred cubic centimeters. The changes in the nonprotein nitrogen were within the limits of error for the method.

The patient's actual condition (at the end of January 1937) showed improvement as compared with that before treatment. He was considerably more in contact with the environment. When talked to he was pleasant and cheerful and answered some questions; even when he remained silent he was in rapport with the interlocutor, smiling and nodding his head in answer to questions. He was also more active than before, reading and being sociable with patients and the hospital personnel. He had stopped soiling. One is justified in speaking of marked improvement.

Weight: Before treatment, on July 8, he weighed 101 pounds (45.8 Kg.), and after treatment, on November 25, 126 pounds (57.2 Kg.),

The patient continued to improve, with increased spontaneous conversation and activity. He was sent home on leave Jan. 24, 1937.

The points of interest in this case are:

1. The relatively high dose of insulin induced for the most part a blood sugar level approximating 50 mg. per hundred cubic centimeters, and only twice such low values as 38 and 20 mg. per hundred cubic centimeters.

2. The most pronounced clinical reactions were associated with levels of blood sugar of about 50, 38 and 20 mg. per hundred cubic centimeters. Again, in this case there is no consistent relationship between the level of sugar in the blood and the reactions.

3. The same dose of insulin had different effects on the amount of sugar in the blood.

4. A distinct, but moderate, therapeutic effect was obtained in an acute condition of only four months' duration.

CASE 4.—E. F., a man aged 25, single, a bank clerk, who was committed on June 10, 1936, to the Spring Grove State Hospital, about Sept. 1, 1935, had become inefficient in his work and had behaved in a peculiar manner. He wasted time in discussing irrelevant business details, misconstrued obviously harmless remarks made in the office and showed resentment toward his superiors. At times he seemed preoccupied. At home he complained that every one was against him. At the beginning of November, in an interview at which he was criticized by the office manager, he launched into a lengthy dissertation on the needs of religion and on his being exposed to the obscene and profane talk of other employees. On the night of January 6 he secured a gun and wanted to go out on the street and "put an end to those dope-pedlers." On January 7 he was admitted to the Henry Phipps Psychiatric Clinic. On admission and for the following forty-eight hours, he showed fear, restlessness and hallucinatory experiences—seeing snakes, wolverines and bats and feeling the bats biting him. The rectal temperature was 101 F. on admission and remained around 100 F. for four days. The tonsils were slightly cryptic and showed some exudate. The blood—except the bromide content of 25 mg. per hundred cubic centimeters—and the cerebrospinal fluid showed no abnormality. The patient said that he heard his name called, that the food was poisoned and that he had a mission to see that people had a square deal. He felt that his mind was being read and that he was being watched. During the next two months he was restless, and combative; he saw animals and heard the voice of God directing him. Then he became mute and remained so most of the time until commitment to the Spring Grove State Hospital, on June 10.

Outstanding Features.—These were: delirium-like condition; delusions of persecution by dope-pedlers and of food poisoning; ideas of reference; hearing the voice of God; restlessness; combativeness, and mutism most of the time for about six months.

Treatment with Insulin.—On September 9, at the beginning of the insulin shock treatment, the patient's condition was unchanged. For the first three days he received 25 units daily. Extreme restlessness and combativeness were the prominent reactions about one hour and a half after the injections. The pulse and respiratory rates and the blood pressure did not change significantly. The patient had his regular lunch from three to four hours after the injections. During the next ten days he received from 40 to 55 units every other day. Motor restlessness was prominent after each injection. On two occasions profuse perspiration and deep sleep were noted. He received dextrose orally and twice intravenously from four to five hours after the injection of insulin. The pulse and respiratory rates had not changed significantly. During the following six weeks the patient had seventeen treatments, at intervals of two or three days, the shock dose being 65 units. The first injection of 65 units was followed by restlessness and then by deep sleep, with biting the tongue, accumulation of mucus

in the throat, generalized rigidity and difficulty in breathing. The pulse remained strong, but the rate fell from 88 to 46 during coma. The shock was terminated six hours after injection of insulin by dextrose, given intravenously and orally. When the patient was aroused he refused to eat and vomited one hour after he had had dextrose. Once insulin was omitted for seven days, during which his condition remained unchanged. When treatment was resumed, the reactions noted were similar to those just described: motor restlessness, perspiration, comatose state, heavy breathing, hypersalivation, biting the tongue, muscular twitchings and marked diminution in the pulse rate, with irregular pulse on two occasions. Perspiration was usually slight or absent. Twice during the period of restlessness he talked: "Why don't you let me go home? Why do you keep me in bed all the time? I am not sick." Then he continued to ramble from one subject to another. After some treatments he was more communicative and helped in the ward more than usual. This, however, was limited to the rest of the day, after termination of the shock. The level of the blood sugar during the treatments varied from 30 to 52 mg. per hundred cubic centimeters. Marked reactions were associated with the two extreme limits of values for blood sugar. Blood was taken during the coma, just before its termination by administration of dextrose.

Weight: On September 9, at the beginning of treatment, the patient weighed 99 pounds (44.9 Kg.); on November 4, 106½ pounds (48.3 Kg.), and on November 25, 102 pounds (46.3 Kg.).

Course.—Since conclusion of the treatment a slight improvement has been sustained. The patient continues to be mute most of the time but is more active. When asked to do work, he does it. Before the treatment he would do nothing. Now he is at times helpful with other patients. Occasionally he talks to his mother, saying, "Glad to see you," "How are brothers?" He never did this before the treatment. To the present (Jan. 26, 1937) the patient's condition has remained essentially unchanged. He wanders about rather aimlessly, talks little, but answers specific questions and does work in the ward when directed to. He went home for Christmas and while there talked freely with his family and friends, seemed to take an interest in the surroundings and behaved almost as he used to before his illness, according to his mother. Since then, however, his behavior has been as previously described.

The points of interest in this case are:

1. A favorable change in behavior, often limited to a few hours, was produced by each treatment.

2. Slight durable improvement occurred in a patient who had been ill about a year.

3. Shock reactions were pronounced and therapeutic results meager.

4. The same dose of insulin—65 units—provoked hypoglycemia, ranging from 52 to 30 mg. per hundred cubic centimeters.

5. Marked reactions were associated with the extreme limits of values for blood sugar, i. e., 30 and 52 mg. per hundred cubic centimeters.

CASE 5.—J. L., a white man aged 60 when the insulin treatment was administered, had been admitted to the Baltimore Psychopathic Hospital in 1921, at the age of 46, with a history of ideas of persecution by members of his family and others for six months. Soon after his admission he became mute and sat

all day with head bowed and hands in his lap, apparently completely indifferent to the environment. He was committed to the Spring Grove State Hospital on Feb. 2, 1922. During his first six years in the hospital, till September 1928, he remained mute but obeyed commands to do work, such as scrubbing, cleaning and sewing. Occasionally he had asthmatic attacks. He had received treatment with horse serum, without improvement. The history of the next eight years in the hospital shows that his condition remained essentially the same: Mutism; sitting with the head bowed on the chest, at times with marked flexibilitas cerea, and apparent complete lack of interest in the environment were the salient features. However, he took food and ate well; he would put out his tongue to have it pricked, but otherwise did not cooperate. His physical condition remained fair, although he was undernourished at the beginning of the treatment with insulin.

Outstanding Features.—These were: mutism; apparent disinterest in the environment; uncooperativeness; marked cataleptic reactions; age, 60 years, and duration of illness, fourteen years.

Insulin Therapy.—The treatment was carried on for two and one-half months. The patient reacted strongly to insulin, the shock dose being only 25 units. Profuse perspiration, excessive salivation, semicomatose state and deep coma were the essential reactions. After certain injections, when aroused by administration of dextrose, he talked for a few minutes: "You are good people. Over there they are going to kill me. They hit me." After another treatment he said: "Good people. They beat me if I talk. They beat me over there. Not here. They beat me a hundred times. Yes, I am hungry." He talked about five minutes. Once, after he came out of coma, he laughed and talked, saying that he remained silent because some one wanted to kill him. Frequently, after the treatments he answered questions with "yes" or "no" or smiled when spoken to, but did not answer. Between the treatments he relapsed into his usual condition. The patient did not benefit from the treatment. There was no change in his psychotic condition except that he spoke for a few minutes after some of the shocks. He has remained mute and cataleptic since termination of the treatment.

Weight: Before July 21 the patient weighed 115 pounds (52.1 Kg.) and after August 27, 117 pounds (53.1 Kg.).

The points of interest in this case are:

1. Hypersensitivity to insulin was shown by the clinical reactions and the hypoglycemia, which on several occasions reached levels of 20, 22, 19 and 18 mg. per hundred cubic centimeters.

2. The same dose of insulin given at various times, but in as nearly similar conditions as possible, provoked a wide range of low values for the blood sugar, the extreme limits being 60 and 18 mg. per hundred cubic centimeters.

3. Notwithstanding the pronounced shock reactions, the therapeutic effect was nil, except for the transitory rapport, including conversation, which followed immediately the breaking up of shock by administration of dextrose.

CASE 6.—T. G., who was committed to the Spring Grove State Hospital from the Baltimore City Jail on Jan. 15, 1932, at the age of 28, had since 1931 been arrested twenty times for disorderly conduct, disturbing the peace and burglary

and had spent most of the time in Maryland House of Correction and the Baltimore City Jail. In the hospital he stated that in July 1930, in the Baltimore City Jail, he heard voices—a woman's voice proposing marriage and a man's accusing him of things he had "done and got away with." He "imagined" that one of the prisoners could keep him between two disks and make him do what he pleased and would know what he was doing and thinking about. "Day and night" he saw his uncle "getting hung." The uncle served a life sentence for murder. The patient continued to hear voices for three months after he left the prison, on Nov. 7, 1930. He had a "hunch people thought he was crazy." On admission to the Spring Grove Hospital, he showed good insight into his condition. The ideas of influence and hallucinations which he had experienced in 1930 made him think that he "was going crazy," and this depressed him.

In the hospital he showed mild depression. With regard to his mother, he said: "Sometimes when I look at her, she looks like my mother, and at other times she looks like a strange woman that I have never seen." He explained that when she was good to him and gave him money she looked like his mother but that when she nagged him she looked like a woman he never saw before. When he demanded sexual relations with her, she did not look like his mother.

During the four years in the hospital he was a good worker in the ward. At times he was excited, disturbing and assaultive. He was always well oriented in all spheres and discussed his past coherently and relevantly, but persisted in his claims that people called him vile names at night and that he heard people or voices making homosexual advances to him.

Outstanding Features.—These were: auditory and visual hallucinations; feelings of passivity; ideas of reference; a long record of disorderly conduct, burglary and imprisonment; delusions of sexual content; age, 32 years, and duration of illness, six years.

Insulin Therapy.—The patient received insulin shock treatment from Sept. 9 to Nov. 20, 1936; from 30 to 50 units caused more or less pronounced perspiration and complaints of abdominal pain, dizziness and hunger. After the treatment he was quiet, cooperative and helpful in the ward. With from 60 to 70 units these reactions were more pronounced; there were, moreover, restlessness and marked salivation and occasionally irregular and slow pulse (from 78 to 48). Termination of one treatment by intravenous injection of dextrose was followed by the patient's inability to grasp or hold objects with the right hand. One hour later he could use the arm slightly; this condition disappeared within three hours. With the successive shock doses of 80 units each the most frequent and conspicuous reactions were excitement and motor restlessness; perspiration and the comatose state were less frequent. Ravenous appetite was a common feature; difficulty in breathing and weak pulse were noted on two occasions. In the intervals between the treatments he was cheerful, cooperative and industrious.

Course.—Before Treatment: The patient was quiet and seclusive, keeping to himself. He was a good worker but needed coaching; he was frequently combative for no apparent reason. He voluntarily sat or walked around, watching everybody closely as if suspicious and looking through the window, but doing nothing and not talking at all spontaneously; if talked to he answered "yes" or "no" and turned away. If told to sweep the room or scrub the floor, he said, "Yes, 'mm" but made no attempt to do so; if handed the implements he did the work as well as a normal person. When the work was finished he left the tools just where the job was completed and wandered around as before. He ate well, and sleep was fair.

During Treatments: There was a remarkable change after each treatment, even after the first shock. He became progressively more responsive to conversation. If asked something he answered relevantly and not with just "yes" or "no," as before. He looked more lively and smiled most of the time. He asked for work spontaneously. Since termination of the treatment (November 20) he has himself been securing the broom and, after sweeping the floor, has put it back in the broom closet. After breakfast, he has been giving morning showers to bed patients, spontaneously. The improvement was noted immediately after the first shock and has gradually increased. He works the whole day without being coached and goes from one job to another without standing around as he did before. During the treatment, between the first two or three shocks, he had fits of temper at night, when bothered by some of the patients. Later, i. e., after four or five shocks and for over two months, he had no outbursts, whereas before the treatment he had them at least once a week.

Weight: On August 13 the patient weighed 137 pounds (62.1 Kg.), and on November 25, 140 pounds (63.5 Kg.).

Patient's Statement (Dec. 1, 1936): "I have lost strength and feel weaker than before treatment, but I do feel a lot better. The environment of the ward has helped me; all helped me each time after the treatment. I don't feel annoyed and am more satisfied; my nerves are not as jumpy. I enjoy the work and feel more ambitious and willing to work, whereas before I was lazy, working without enjoying it."

At the time of recording these notes (Jan. 26, 1937), the patient's improvement has continued and is sustained. He works a full day in the ward, expresses no delusions or hallucinations and shows no ill temper and no tendency toward psychopathic behavior, as before the so-called beginning of the acute illness. He is quiet and polite at all times and has recently gone home with his family, expecting to go to work immediately.

The points of interest in this case are:

1. Distinct improvement in a psychopathic person who had displayed schizophrenic features now and then for six years.

2. Relatively mild reactions associated with a low level of the blood sugar of 33 mg. per hundred cubic centimeters. After the patient received dextrose intravenously, he had paralysis of the right arm, which gradually disappeared within three hours.

3. Pronounced reactions associated with a low level of the blood sugar of 46 mg. per hundred cubic centimeters.

COMMENT AND SUMMARY

The limited number of patients treated and the short period which has elapsed since termination of the treatments render premature any conclusive judgment on the therapeutic merits of Sakel's therapy. Such reservations are not justified, however, with regard to the varied reactions of our patients to the injections of insulin, since each patient received numerous injections. Some of the responses to individual treatments varied from one patient to another; also in the same patient the reactions varied somewhat from one injection of insulin to another.

On the other hand, strikingly similar reactions and similar relationships of reactions were observed not only in the same patient in individual treatments but also in the different patients throughout their treatment. The marked repetitiousness, if not fair consistency, of both the physiologic and the personality reactions of our patients to insulin made it possible to condense the reactions under "points of interest" outlined at the end of each case record. These succinct outlines lend themselves to a brief summary of what we regard as noteworthy observations.

1. Favorable therapeutic results were obtained in four patients with a procedure which differs from Sakel's original procedure in several particulars: (1) The total period of treatment was frequently shorter; (2) the injections of insulin were usually given not six times a week but at intervals of two or three days, and (3) the fourth therapeutic phase (polarization phase of Sakel) was not used.

2. In one patient (case 1) a remission was obtained with treatment of only one month's duration. There was a relapse nearly three months after the end of the treatment. The hypoglycemia following injections of insulin remained moderate throughout the treatment.

3. There were discrepancy and lack of consistent relationship between the dose of insulin and the severity of the reactions in all patients. Marked hypersensitivity to insulin was present in one patient (case 5), for whom the shock dose of insulin was only 25 units.

4. There were disproportion and lack of consistent relationship between the amount of insulin and the degree of hypoglycemia in all patients.

5. There were discrepancy and lack of consistent correlation between the intensity of the reactions and the degree of the hypoglycemia in all patients.

VESICAL ACTIVITY IN SCHIZOPHRENIC STATES ASSOCIATED WITH CATALEPSY

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In recent years increasing attention has been paid to the bodily changes that occur in mental disease.[1] Our particular interest in this interrelationship has been directed toward an evaluation of the alterations in muscle tonus in catatonic schizophrenia associated with catalepsy. Since a practical quantitative method of studying the tonus of striated muscle was not available, we planned to study the response of smooth muscle. One of us (O. R. L.) and his associates devised a graphic recording apparatus for determining vesical activity. The bladder was accordingly utilized in this investigation. A series of observations on disturbances of micturition accompanying various organic abnormalities of the nervous system has been described in previous papers.[2] More or less characteristic physiologic changes were observed to be associated with damage to particular cell groups and fiber tracts.

The method employed in the study has previously been standardized and has served as an acceptable technic. It has afforded, furthermore, a measuring rod for making a comparison of vesical function in our

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From the Henry Phipps Psychiatric Clinic; the James Buchanan Brady Urological Institute, and the Sub-Department of Neurology, the Johns Hopkins Hospital.

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patients and that observed in the normal subject and in persons with organic disease of the nervous system.[3]

METHODS

The apparatus consists of a urethral catheter which is connected with an irrigation flask and a simple, sterilizable air-water manometer by means of a T tube. This, in turn, is attached to a tambour for obtaining a graphic record on a smoked kymographic drum. The instrument is so sensitive that respiratory waves are recorded.

The patient is placed on a flat table and instructed to remain quiet, avoiding movements of the abdominal wall and the extremities. He is then catheterized under aseptic technic. The reservoir is filled with sterile water, and all trapped air is expelled from the system. The zero level is set at the symphysis pubis. The pressure in the empty bladder is recorded first. Fluid is added in increments of 50 cc. These additions are made at intervals, when the pressure as registered on the drum has reached a stationary resting level. The pressure of the fluid entering from the reservoir is about 30 cm. of water.

The method makes it possible to chart the intravesical pressure at different volumes, the reaction of the bladder to sudden stretch and the activity of the voiding reflex. The graphic record also permits the study and comparison of a series of readings.

NORMAL READINGS

A number of records obtained from normal persons complaining of no vesical or neurologic symptoms have been collected previously. The capacity of the normal human bladder is about 500 cc. A graph for one of the normal subjects appears in figure 1. The vertical lines on the graph record the sharp rises of pressure accompanying the sudden introduction of increments of fluid into the system. The pressure in the empty bladder was about 1 cm. of water. The pressure was 3.5 cm. when the bladder held 50 cc. and remained below 7 cm. until 500 cc. had been introduced and filling was completed. After each quanitity of fluid had entered the bladder, the pressure dropped at once to a resting level and maintained it. No waves of muscular contraction occurred during the filling. At a volume of 250 cc. the subject first became aware of vesical distention, and a slight irregularity in the curve at this point was associated with speaking. The pressure was slow in reaching a resting level with a volume of 500 cc. A marked contraction of the muscle raised the pressure to 54 cm.; at this time fluid escaped from the urethra around the catheter.

3. The staff of the Spring Grove State Hospital, Catonsville, Md., gave us permission to study their patients and to use their facilities.

SELECTION OF MATERIAL FOR STUDY

Patients suffering from catatonic schizophrenia who exhibited varying degrees of catalepsy were studied. Selection of the material was based on the predominance of disturbances in motility observed in the patients. Correlation between the extent of the catalepsy and the alteration of tonus in the detrusor muscle was considered possible. If the patient expressed by word or attitude any uneasiness during the study, the cystometric reading was immediately terminated, in view of the possible tendency to overconcern and preoccupation with the body.

During the cystometric reading the cataleptic patients assumed an unusual posture, which may best be called the "steamer chair" position. This exhausting attitude was maintained throughout the

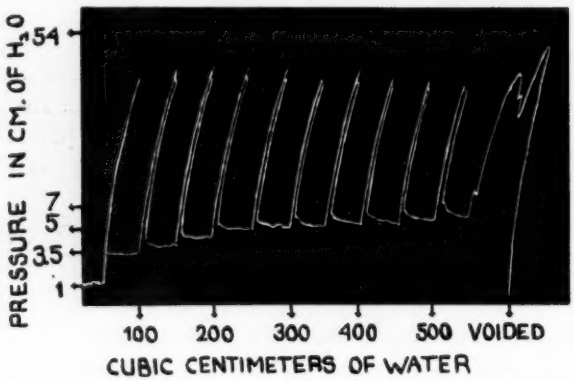

Fig. 1.—Graph of intravesical pressure for a normal person.

experiment. The buttocks and the heels were virtually the basis of support. The neck and shoulders were elevated several inches from the table. The knees were held flexed at an angle of from 25 to 45 degrees, while the arms were adducted and flexed at the elbows. As a rule there was little inclination to rest the elbows on the table. The fists were often clenched. This awkward, energy-consuming posture not infrequently provoked the development of fine generalized tremors of the body musculature. The patients were remarkably quiet during the study, and only at times could one notice an inappropriate smile or grimace cross the face.

Careful neurologic examination of each patient revealed no disturbance other than the catalepsy. No complaints related to the functioning of the urinary bladder were elicited. Most of the patients were mute; however, the nursing records revealed no evidence of frequency, nocturia or continual incontinence. The incontinence

encountered in certain patients was considered functional, such as that in persons who soil the ward after having previously been assisted to the lavatory.

The normal person usually experiences great discomfort when the bladder reaches its capacity. The fluid is then seen to rise in the manometer, and there is leakage of urine around the catheter. If the bladder is not emptied at this stage, the addition of more fluid produces sufficient stress to initiate micturition. Most persons agree that it is difficult to prevent micturition, even by great effort. In many of our patients, on the other hand, there were no sharp reflex waves when the bladder was approaching its capacity. When the patient was requested to void if he felt uncomfortable, there was no indication of sufficient rise in pressure in the manometer to inaugurate micturition. Even though the pressure was then raised to a high level, there was no

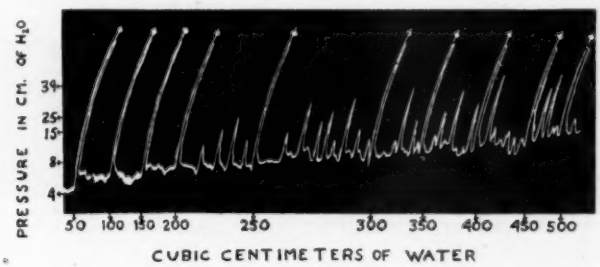

Fig. 2.—Record of vesical filling in case 1.

reflex response of the muscle of the bladder and no escape of fluid from the urethra. In these persons a great deal of resistiveness and negativism was observed.

REPORT OF CASES

CASE 1.—J. H., a white man aged 20, the son of a paranoid, litigious mother, was first seen five years ago, when he complained of numerous strange body sensasations. Within the next few years periods of unexplained excitement, with incoherent and irrelevant speech and asocial behavior, resulted in his commitment to a state hospital. In June 1936 the patient suddenly became mute, refused to eat, assumed rigid postures and was unresponsive in every way.

The cystometric reading was made approximately two months after the onset of catalepsy. Figure 2 shows the record of vesical filling. The resting intravesical pressure was 4 cm. of water. The pressure was maintained at from 4 to 8 cm. of water until the bladder held over 200 cc. of fluid. Numerous reflex waves of vesical contraction appeared at this point and increased in size and frequency. The largest of these waves raised the pressure to from 15 to 39 cm. of water. Even at a pressure of 39 cm. there was no escape around the catheter of fluid from the urethra. With a volume of 500 cc. and a pressure of 25 cm. the patient became uncomfortable, and his eyes filled with tears; the

experiment was terminated at this point. There never was escape of fluid around the catheter, although the patient was requested to empty his bladder as soon as he experienced discomfort.

CASE 2.—T. B., a white man aged 40, was admitted to a state hospital at the age of 22, after having suffered a nervous breakdown characterized by overtalkativeness, unprovoked laughter, confusion and apparent exaltation. His tendency to wander about poorly clad led finally to commitment. Once hospitalized, he became untidy, lost interest in his surroundings and spoke of there being holes in his body and of his organs being removed. In the next few years he became mute, assumed awkward postures and was incontinent and out of contact with reality. The extreme rigidity of the skeletal muscles has been observed for fifteen years.

The resting pressure in the empty bladder was 2 cm. of water (fig. 3). After the introduction of 50 cc. of fluid a strong vesical contraction, following a short latent period, raised the intravesical pressure to 64 cm. Thereafter, waves of muscular contraction occurred at equally spaced intervals after the inflow of increments of fluid to the bladder. These waves were different from the stretch reflex seen in organic disease of the nervous system in that they appeared after a definite latent interval. Furthermore, there was never any escape of fluid from

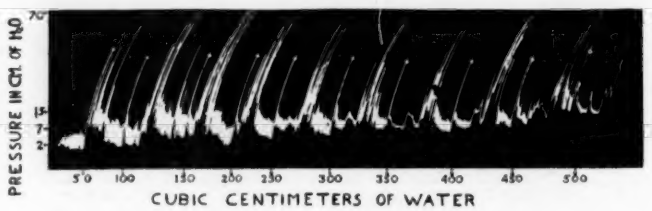

Fig. 3.—Record of vesical filling in case 2.

the urethra, even though the pressures reached levels as high as 64 cm. When the bladder reached a volume of 500 cc., the patient was instructed to void. The pressure then rose slowly to 70 cm., and fluid escaped around the catheter. The large excursion of the respiratory waves seen in the record was due in part to the taut adjustment of the tambour.

CASE 3.—M. S., a white woman aged 24, who had been admitted to the state hospital four years before, had been an unwanted child, rejected and neglected by immediate and remote kin. She was deserted by a lover and gave birth to a baby in May 1932; three days later she became excited and restless and had ideas that people were against her. She rapidly became inactive and mute, had to be fed with a spoon, soiled herself and showed marked catalepsy. The cystometric reading was made approximately four years after the onset of catalepsy.

The vesical record in this case is seen in figure 4. The resting intravesical pressure in the empty bladder was 5 cm. of water. Before the introduction of any fluid numerous reflex waves of vesical contraction were observed. The pressure at the peaks of the larger waves varied from 35 to 45 cm. of water; there was no escape of fluid from the urethra. Fifty cubic centimeters of fluid was then introduced into the bladder, and once more the waves occurred. The pressure reached 62 cm. of water without any escape of fluid. As water was added in equal quantities, the waves continued to appear, but the strength of the contraction decreased steadily. The waves of vesical contraction appeared periodically. At

a volume of 250 cc. of fluid, with an intravesical pressure of 13 cm., the patient seemed distressed, and the experiment was terminated. Micturition did not occur.

CASE 4.—R. S., a white woman aged 25, unmarried, who was admitted to a state hospital in 1933, was described by relatives as a quiet, lonely soul, with narrow interests; she was first seen shortly after the close of a thwarted love affair. She complained of poor sleep and imagined people "had it in for her." She was fearful, excited and actively hallucinated. Her stream of talk was irrelevant. She quickly lapsed into an unresponsive state, drooled saliva, soiled and had to be fed with a tube. Catalepsy had been observed for the last three years.

Study of the bladder revealed the following: The resting intravesical pressure in the empty bladder was 6 cm. of water. The pressure rose approximately 1 cm. after the introduction of each increment of 50 cc. of fluid, so that there was a gradual rise of intravesical pressure throughout filling. When the bladder held 450 cc., the intravesical pressure was 12 cm. of water. At that point and thereafter, a stretch reflex was seen to occur before complete accommodation of the bladder following the inflow of fluid. When the bladder held 750 cc. the pressure was 21 cm., and just before the next filling two waves of vesical contraction raised the pressure to 32 cm. This response was duplicated after 800 cc. of fluid was present in the bladder, and this time the pressure reached 34 cm.

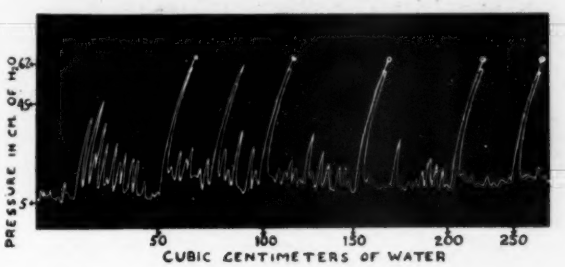

Fig. 4.—Record of vesical filling in case 3.

of water. There was no escape of fluid at this pressure, nor was there any when the bladder held 850 cc. of fluid, at an intravesical pressure of 26 cm. The reading was discontinued at this point because of the discomfort experienced by the patent.

CASE 5.—J. F., an Italian farm lad aged 16, with a seventh grade education, who was admitted to the hospital in 1936, was described by his parents as a sensitive, touchy boy, who was easily upset by the slightest deprivation. His illness began suddenly in the form of a panic reaction with great fear, bewilderment and visions of a threatening nature. The patient sought help and was greatly agitated over imperative auto-erotism. He quickly became mute, resistive and cataleptic. The cystometric reading was made three months later.

The resting intravesical pressure in the empty bladder was 2 cm. of water. After 50 cc. of fluid was introduced, the pressure rose to 4 cm. A reflex wave then raised the pressure to 8 cm. The intravesical pressure dropped to 4 cm. After the introduction of the next 50 cc. of fluid a few small waves of vesical contraction raised the pressure to 12 cm. of water, after which the intravesical pressure again registered 4 cm. No more waves occurred during the rest of the experiment. The intravesical pressure was 12 cm. when the bladder held 600 cc. of fluid. After the addition of the next 50 cc. a stretch reflex raised the pressure to 80 cm. of water, and fluid escaped for the first time from the urethra.

CASE 6.—J. L., a Polish laborer aged 60, who was picked up on the streets by the police in 1922, had been under state hospital surveillance for fourteen years. He was homeless; no relatives claimed him. The patient at first was deeply depressed, showed no interest in his surroundings and rarely talked. No adequate history was available. During the early years of hospitalization ideas of persecution were prominent, and there was much antagonism. Automatic obedience and waxy flexibility, with mutism and catalepsy, followed shortly. The muscular rigidity, although present from the onset, had become more marked in the last eight years.

The resting intravesical pressure was 2 cm. of water. The pressure in the bladder rose slowly and measured 7 cm. when 300 cc. of fluid was present. After each addition of fluid, even the initial inflow, a small stretch reflex was seen to occur before the muscle of the bladder showed complete accommodation to the fluid introduced. The stretch reflex following subsequent incremental additions was stronger. The resting pressure was above 10 cm. after the bladder held 400 cc. The bladder held 550 cc. of fluid at an intravesical pressure of 26 cm. After the introduction of the next 50 cc. there was a sudden rise of pressure to 80 cm. of water, and fluid escaped from the urethra.

CASE 7.—J. S., a white woman aged 48, married, who was admitted to the state hospital eight years ago because of attempted suicide, was described as suspicious, querulous and inflexible. The mental content in her illness consisted of ideas of the infidelity of her husband and assertions that neighbors put strange objects into her stomach and that all her belongings were stolen from her. Neglect of personal habits was prominent. Within a short time she lost interest in everything about her and became progressively less responsive. Catalepsy had been observed for approximately eight years.

The resting intravesical pressure was 6 cm. of water. Equal increments of fluid were introduced, and after a short latent period a small wave of vesical contraction occurred, each time raising the pressure to about 12 cm. of water. The bladder held 400 cc. of fluid at a pressure of 15 cm. of water. Because the patient showed signs of discomfort, the experiment was then terminated. At no time was the intravesical pressure high enough to produce escape around the catheter of fluid from the urethra.

CASE 8.—L. T., a white woman aged 29, married, who has been institutionalized for one and a half years, became mentally ill while her oldest son was slowly recovering from a grave wasting disease. The patient feared she might die and that some external force would remove the boy and her other children from her. There were episodes of impulsiveness, combativeness and unleashed fury, which resulted in her commitment. Her behavior in the hospital was asocial; she talked rarely, walked about with a sullen, defiant air and showed mild catalepsy.

The resting intravesical pressure was 1 cm. of water. The cystometric reading was essentially normal. The pressure was low throughout the study and was only 4 cm. of water when the bladder held 650 cc. of fluid. At this point the experiment was interrupted because the patient became uncomfortable. No fluid escaped from the urethra. There were no abnormal waves of vesical contraction.

CASE 9.—P. M., a white woman aged 31, married, was admitted to the hospital in 1934, one month after the birth of her child. She showed no interest in the child and neglected it but became excited and angry when any one approached it. She wandered about the streets, misidentifying persons and places and accusing people of controlling her. After hospitalization she showed a mild degree of catalepsy. This case is the second in which the extent of the muscular rigidity was slight.

The resting intravesical pressure was 3 cm. of water. After the introduction of equal increments of fluid into the bladder the intravesical pressure rose slowly to 10 cm. of water. When the bladder held 350 cc. there was a sudden stretch reflex, with rise of pressure to 85 cm. of water and escape of fluid around the catheter. There were no abnormal waves of vesical contraction in this case.

CASE 10.—C. R., a white woman aged 31, who had been unhappily married, divorced and remarried, was admitted to the state hospital two years ago because she had the notion that she was under suspicion for premeditated murder and claimed that she was being influenced, that the food was poisoned and that her body had rotted away. She was troubled with distressing olfactory hallucinations. There was inappropriate affect, with scattering, neologisms and verbigeration. There was no disturbance in motilty. This case is included to illustrate the response of the muscle of the bladder in the noncatatonic group of schizophrenic patients.

The record of vesical filling is seen in figure 5. The resting intravesical pressure was 2 cm. of water. There was a gradual increase in intravesical pressure as increments of 50 cc. of fluid were introduced into the bladder. The four slight irregularities in the smooth reading were due to voluntary movement and laughing

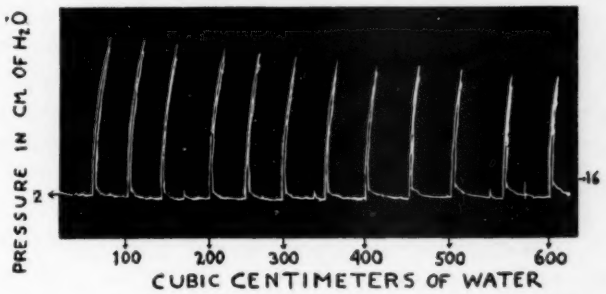

Fig. 5.—Record of vesical filling in case 10, that of a schizophrenic patient without catatonia.

on the part of the patient. At a volume of 600 cc. the pressure was 16 cm. of water. The patient became uncomfortable at this point, and the experiment was interrupted. The intravesical pressure was never sufficient to produce escape of fluid from the urethra.

COMMENT

Nine cases of catatonic schizophrenia in which varying degrees of catalepsy were shown and one case of the noncatatonic type are analyzed from the standpoint of the response of the muscle of the bladder to filling. In the first seven cases catalepsy was marked, and it was primarily in this group that abnormal reactions were observed. The initial intravesical pressure in the empty bladder was, as a rule, within normal limits, but the pressure increased rapidly and revealed an unusually high resting level after the addition of fluid. The next conspicuous feature was the appearance of numerous waves of vesical contraction unassociated with voluntary movement or speech on the part of the patient. It was common for waves of muscular contraction

to carry the intravesical pressure to 60 cm. of water without escape of fluid from the urethra. In some cases reflex contractions occurred after each introduction of fluid into the bladder. If these were responses to stretch, they showed a considerable latent period. Finally, the bladder in these cases had a greater capacity than is commonly observed in the normal person.

The patients did not initiate micturition even when the vesical pressure was high. They may have been able to exert sufficient effort to keep the external sphincter, a voluntary muscle, contracted and thereby prevent the escape of fluid around the catheter.

The records obtained from these patients may be compared with those previously obtained for another group of persons with injury of certain localized pathways in the central nervous system. It is clear that after injury of the efferent fibers from the cerebral cortex the vesical capacity is small and the resting intravesical pressure high.[2a] Further injury of efferent pathways from the brain, particularly the descending path from the midbrain which appears to control tone in the vesical muscle, releases rhythmic waves of vesical contraction which are observed throughout the entire period of filling. These waves are also observed after severe injury of the spinal cord and damage to the anterior sacral nerve roots, as in spina bifida. The spontaneous waves seen in some of the cases resemble those seen after injury of the efferent pathways from the brain.

In certain patients with the parkinsonian syndrome the resting intravesical pressure has been found to be abnormally high during the period of filling.[2a] Indeed, this resting pressure may exceed that which causes imperative micturition in the normal subject.

When the reflex arc is injured on the sensory side, by interruption of either the posterior roots or the ascending pathways in the cord or brain, there is decreased tone in the wall of the bladder and the vesical volume is increased.[2c, d] Here again, there is similarity to patients in the cataleptic group, in whom the volume of the bladder is larger than is usual in the normal person.

It is clear that under certain circumstances each abnormality of the bladder observed in the patients in this series has been found in other persons after demonstrable injury to tracts in the nervous system. They have never been seen together in the pattern observed here.

The resting intravesical pressure in the empty bladder of a normal person is never zero, but it is probably never greater than 2 cm. of water. The normal person feels a strong desire to micturate before the pressure reaches 10 cm. of water. In this series the pressure rose even to 60 cm. of water without eliciting the emptying reflex.

It may be argued that contraction of the abdominal muscles is responsible for the high intravesical pressure. It is more probable

that the increased pressure is due to physiologic changes in the smooth fibers of the detrusor muscle. Five cats were given from 80 to 100 mg. of bulbocapnine, producing marked catalepsy. In the graphic records of vesical activity the resting intravesical pressure was uniformly high.

Patients with parkinsonism hold fluid in the bladder at high resting pressures, and in certain cases spontaneous waves of vesical contraction are seen.[2a] Records of these contractions resemble those obtained in the present group more than those in other series of patients with organic lesions of the nervous system. Certain authors [4] have compared the findings in catatonic schizophrenia associated with catalepsy with those in the parkinsonian syndrome. While the posture has similarities on superficial examination, this analogy must not be labored.

These findings lead to consideration of the significance of the results. First, we have found that there is an alteration in the response of the muscle of the bladder in the cataleptic group of patients with catatonic schizophrenia. This abnormal response, however, is observed definitely only in cases in which the catalepsy is of large magnitude. The degree, and not the duration, of the catalepsy has been found to be the important criterion of the presence of altered activity in the muscle of the bladder.

SUMMARY

Cystometric readings were made on nine patients with catatonic schizophrenia associated with catalepsy. The resting intravesical pressure was usually high during filling of the bladder. Abnormal waves of contraction of the muscle were observed. The bladder in these cases had a greater capacity than normal. Although waves of contraction carried the pressure to 60 cm. of water, no fluid escaped from the urethra. The patients showed no ability to produce voluntary contraction of the muscle at the end of filling. The records showed distinct deviations from the normal. The changes in the vesical activity paralleled the degree of catalepsy.

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VELOCITY OF BLOOD FLOW IN SCHIZOPHRENIA

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Our purpose in this study was to determine the rate of blood flow in patients with schizophrenia. The work of Blumgart [1] has stimulated interest in studies on the velocity of blood flow. The circulation time, while it does not directly determine the velocity of blood flow, is the denominator in the equation $\frac{\text{distance of pathway}}{\text{circulation time}}$ equals velocity of blood flow. It is assumed that, for practical purposes, the distance of a specific pathway is constant in different persons. Hence, the circulation time can be considered inversely proportional to the velocity of blood flow. In our work the sodium cyanide method of Robb and Weiss [2] was used. The reasons that it is preferable to many other methods were given in their paper.[2] Loevenhart, Lorenz, Martin and Malone,[3] using the sodium cyanide method, reported a number of determinations of the circulation time (latent period, in their terminology) in a patient with schizophrenia, in whom the average value was normal. Freeman [4] reported an abnormally slow circulation in patients with schizophrenia, using the technic of Robb and Weiss.[2] It seemed important to study the cause of this slowing of circulation and to determine whether it occurs in the pulmonary or the peripheral circulation or both.

From the Department of Diseases of the Nervous System and the Department of Obstetrics, the Harvard University Medical School, the Boston Psychopathic Hospital, and the Massachusetts General Hospital.

1. Blumgart, H. L.: The Velocity of Blood Flow in Health and Disease: The Velocity of Blood Flow in Man and Its Relation to Other Measurements of the Circulation, Medicine **10**:1, 1931.

2. Robb, G., and Weiss, S.: A Method for the Measurement of the Velocity of the Pulmonary and Peripheral Venous Blood Flow in Man, Am. Heart J. **8**: 650, 1933.

3. Loevenhart, A. S.; Lorenz, W. F.; Martin, H. G., and Malone, J. Y.: Stimulation of the Respiration by Sodium Cyanide and Its Clinical Application, Arch. Int. Med. **21**:109 (Jan.) 1918.

4. Freeman, H.: The Arm-to-Carotid Circulation Time in Normal and Schizophrenia Subjects, Psychiatric Quart. **8**:290, 1934.

TECHNIC

The technic was described in detail by Robb and Weiss [2] in their paper introducing the sodium cyanide method for the study of the velocity of blood flow in human subjects. In brief, it consists of measuring the time in seconds required for a solution of sodium cyanide injected into a vein to cause a characteristic change in respiration. The change in respiration is associated with stimulation of the carotid sinus. In other words, the time which is required by the blood stream to carry the sodium cyanide from a vein to the site of stimulation in the carotid sinus is measured. When the injection is made into an antecubital vein, the time obtained is referred to as the arm to carotid (A-C) circulation time. Another value determined is the crude pulmonary circulation time. This is the time required for the blood steam to carry the sodium cyanide from the external jugular vein to the site of stimulation of the carotid sinus. This value is considered a crude measure of the velocity of blood flow in the lesser or pulmonary circulation. The arithmetical difference between the arm to carotid circulation time and the crude pulmonary circulation time is designated as the venous circulation time, which is a measure of the velocity of the circulation in a segment of the greater or peripheral circulation.

Most of the tests were carried out on patients at the Boston Psychopathic Hospital. Tests were made on a small number of patients at the McLean Hospital, Waverley, Mass., and at the Massachusetts General Hospital. These determinations were carried out on patients during basal conditions, that is, with the patient without breakfast and lying in bed for at least one-half hour. The pulse was counted, and blood pressure readings were taken by a sphygmomanometer immediately before each test. A 2 per cent solution of procaine hydrochloride without epinephrine was infiltrated into the skin at the site of puncture. A tourniquet was placed around the arm, and an antecubital vein was punctured. The tourniquet was then released, and after a short period the sodium cyanide was injected as rapidly as possible. The time from the beginning of the injection until the specific respiratory response was measured with a stop-watch. This end-point could be accurately determined by observing the abrupt change in respiratory rhythm [2] caused by the stimulation of the carotid sinus by the sodium cyanide. Other evidences of the reaction, such as flushing of the face, onset of blinking and increased pulse rate, were also observed. During the entire test the pulse was counted by a second observer. After an interval of about five minutes, when as a rule the pulse rate had returned to its basal value, the injection was repeated. If the pulse rate had not returned to its basal value, a few minutes more were allowed to elapse before a second injection was made. If the first response was not adequate, the dose was increased by from 2 to 3 mg. in the second injection. The procedure was repeated until results were obtained which checked within two seconds. The precision of the test is not greater than two seconds; therefore, values which were within two seconds of each other were considered a check. After the arm to carotid circulation time had been determined, the crude pulmonary circulation time was obtained by introducing sodium cyanide into the external jugular vein and reading for the time as already described.

SOURCES OF ERROR

There are several possible sources of error in carrying out the determination of the circulation time by this method.

1. It is important to administer the optimal dose of sodium cyanide to each patient. This optimal dose is, by definition, the smallest dose which will give the smallest arm to carotid value, expressed in seconds. An increase in the amount beyond the optimal dose will not change the arm to carotid or the crude pulmonary circulation time. A dose smaller than the optimal, however, might give a greater value for the circulation time. Beginning with a reasonably small dose, it is important to increase the amount of sodium cyanide injected until the optimal dose is reached. The optimal dose is then repeated as a check. It is impossible to be sure of the circulation time by giving a single injection. If an amount smaller than the optimal dose is given, the values for the circulation time are greater, and the blood velocity is falsely determined.

2. It has been the experience in this investigation, as well as in that of Weiss,[5] that in some patients the first dose of sodium cyanide administered required a longer time to give the respiratory response than did the same amount of sodium cyanide in subsequent doses. At present there is no explanation for this phenomenon. Weiss [5] suggested that the carotid sinus mechanism is in some way sensitized by the first dose. As a result of this phenomenon, which occurs in some patients, the first measure of the blood velocity cannot be considered reliable unless it is checked by a subsequent measurement. We have found that an average error of 17 per cent in sixty-four cases of miscellaneous psychiatric conditons could be accounted for through this source of error, with large errors in individual cases.

3. There appears to be a negative correlation between the pulse rate and the circulation time in a series of patients. Hence it is important to wait after the first injection until the pulse rate has returned to its basal level before the next injection is repeated, in order to avoid this as a possible source of error.

NORMAL VALUES

Before attempting to determine whether there is any abnormality in circulation time in patients with schizophrenia, it is important to consider the data available as to the values of the arm to carotid and crude pulmonary circulation times in persons used as controls. Of the various methods employed in measuring the circulation time, the decholin method [6] is the most comparable to the sodium cyanide method. The decholin method has a distinct disadvantage in that the end-point of the reaction is determined by having the patient report a bitter taste. This

5. Weiss, S.: Personal communication to the authors.

6. Winternitz, M.; Deutsch, J., and Brüll, Z.: Eine klinisch brauchbare Bestimmungsmethode der Blutumlaufszeit mittels Decholininjektion, Med. Klin. **27:** 986, 1931.

introduces a subjective factor, which is avoided by the sodium cyanide method. In working with psychotic patients it is especially important to use a method which does not rely on the subjective impression of the patient.

The normal values are presented in table 1. It is apparent that there is a certain amount of agreement among the various authors. The investigators using the sodium cyanide method, with the exception of Freeman,[4] found average values of 15.6, 15.6 and 15.7 seconds, respec-

TABLE 1.—*Determinations of the Normal Circulation Time by Various Authors, Using the Radioactive, Decholin and Sodium Cyanide Methods*

Authors	Method	Pathway	No. of Patients	Average Dose, Mg.	Average Value, Sec.	Range, Sec.
Blumgart and Weiss [7]....	Radioactive	Arm to arm	53	..	18.0	14-24
Blumgart and Weiss: J. Clin. Investigation **4**: 399, 1927	Radioactive	Jugular vein to arm	62	..	10.8	5-17
Winternitz, Deutsch and Brüll [6]	Decholin	Arm to tongue	..	..	....	8-14
Gargill: New England J. Med. **209**: 1089, 1933	Decholin	Arm to tongue	50	..	15.9	15-20
Gargill: New England J. Med. **209**: 1089, 1933	Decholin	Jugular vein to tongue	12	..	13.2	12-15
Tarr, Oppenheimer and Sager: Am. Heart J. **8**: 766, 1933	Decholin	Arm to tongue	60	..	13.0	10-16
Macy, Claiborne and Hurxthal: J. Clin. Investigation **15**: 37, 1936	Decholin	Arm to tongue	14	..	12.8	9-18
Robb and Weiss [2].....	Sodium cyanide	Arm to carotid sinus	35	7	15.6	9-21
Robb and Weiss [2].....	Sodium cyanide	Jugular to carotid sinus	21	4	10.6	7-14
Gargill: New England J. Med. **209**: 1089, 1933	Sodium cyanide	Arm to carotid sinus	15	8	15.6	12.5-18
Freeman [4]	Sodium cyanide	Arm to carotid sinus	26	8	21.9	12-40
Cohen and Thomson:* J. Clin. Investigation **15**: 607, 1936	Sodium cyanide	Arm to carotid sinus	19	7	15.7	12-24

* In nineteen normal patients, seventeen of whom were referred to by Cohen and Thomson (J. Clin. Investigation **15**: 607, 1936), the actual values for the arm to carotid circulation time were 12, 12, 12, 13, 14, 14, 15, 15, 15, 16, 17, 17, 17, 17, 17, 18, 19, 20 and 24 seconds.

tively, for the arm to carotid time. Freeman [4] found that for the staff and employees of the Worcester State Hospital the average normal arm to carotid value was 21.9 seconds, a figure greater than that reported by various other investigators using the sodium cyanide method. Robb and Weiss [2] also reported that the average normal crude pulmonary circulation time is 10.8 seconds. The figures for the decholin method averaged from 12.8 to 14 seconds for the arm to tongue circulation time. The radioactive method as used by Blumgart and Weiss [7]

7. Blumgart, H. L., and Weiss, S.: Studies on the Velocity of Blood Flow: The Velocity of Blood Flow in Normal Resting Individuals, and Critique of Method Used, J. Clin. Investigation **4**:15, 1927.

TABLE 2.—*Velocity of Blood Flow and Related Data for Patients with Schizophrenia*

Case No.	Sex	Age, Yr.	Weight, Lb.	Known Duration of Disease		Pulse Rate During Fasting	Arterial Blood Pressure, Mm. Mercury		Pulse Rate During Test		Hemoglobin, %	Basal Metabolic Rate	Dose Sodium Cyanide, Mg.		Circulation Time, Sec.			Psychiatric Diagnosis	Physical Status
				Yr.	Mo.		Systolic	Diastolic	Initial	Maximum			Arm to Carotid	Pulmonary	Arm to Carotid	Pulmonary	Venous		
1	M	21	127	5	..	84	110	84	..	...	90	+11	6.4	5.2	18	11	7	Hebephrenic schizophrenia	Normal
2	M	23	121	..	6	62	100	55	62	...	90	—15	6.4	6.0	19	11	8	Schizophrenia	Old tuberculosis of hip
3	M	36	125	2	..	66	115	70	68	96	70	....	8.0	7.0	16	11	5	Paranoid schizophrenia	Left pupil larger than right
4	M	50	154	15	..	62	102	64	62	...	90	....	6.0	...	15	..	..	Paranoid schizophrenia	Arteriosclerosis
5	F	37	166	6	..	88	115	80	..	...	85	—11	5.0	4.8	12	9	3	Paranoid schizophrenia	Normal
6	M	31	146	4	..	56	110	70	84	...	90	— 2	7.6	7.2	26	15	11	Schizophrenia	Normal
7	M	15	112	1	..	60	104	50	64	96	..	....	8.0	6.0	18	11	7	Paranoid schizophrenia	Normal
8	M	39	117	10	..	52	120	80	56	56	80	—27	7.4	6.0	19	14	5	Paranoid schizophrenia	Rheumatic heart disease
9	F	36	120	..	½	72	120	70	68	108	80	....	7.0	6.0	16	10	6	Paranoid schizophrenia	Rheumatic heart disease
10	F	39	121	5	..	96	130	86	96	112	85	....	6.0	5.6	13	9	4	Hebephrenic schizophrenia	Rheumatic heart disease
11	M	25	160	1	..	80	120	75	80	100	85	....	7.8	7.0	16	13	3	Schizophrenia	Myopia
12	F	39	166	5	..	76	130	75	76	102	90	....	6.6	6.0	11	9	2	Schizophrenia	Normal
13	F	36	115	7	..	80	102	65	80	100	80	....	5.0	5.0	13	10	3	Paranoid schizophrenia	Normal
14	F	40	97	5	..	82	150	90	88	100	75	....	5.8	5.0	13	9	4	Paranoid schizophrenia	Normal
15	M	53	173	5	..	88	130	75	72	84	80	....	5.8	5.4	11	9	2	Paranoid schizophrenia	Generalized arteriosclerosis
16	F	15	99	..	6	70	115	65	68	112	90	....	5.7	...	12	..	..	Hebephrenic schizophrenia	Normal
17	F	22	...	..	9	54	100	55	66	112	90	+ 1	7.6	6.8	17	11	6	Paranoid schizophrenia	Sinus arrhythmia
18	M	52	132	..	..	..	140	75	56	56	80	—31	6.0	...	15	..	..	Hebephrenic schizophrenia	Normal
19	F	31	80	2	..	76	130	55	80	100	60	....	5.8	4.8	11	9	2	Schizophrenia	Normal
20	F	42	147	8	..	64	98	72	64	88	80	—21	6.6	6.0	15	11	4	Paranoid schizophrenia	Normal
21	F	31	128	5	..	86	140	72	100	120	55	+30	6.6	6.0	12	9	3	Paranoid schizophrenia	Normal
22	M	49	200	3	..	48	90	55	44	60	80	— 8	8.0	7.6	18	16	2	Paranoid schizophrenia	Normal
23	F	22	125	2	..	92	122	80	76	132	85	....	7.0	...	12	..	..	Catatonic schizophrenia	Normal
24	M	44	111	..	1¼	72	110	72	72	72	90	....	6.4	5.8	16	14	2	Paranoid schizophrenia	Pulmonary emphysema

25	M	48	111	..	..	42	150	80	54	62	80	....	6.0	6.4	17	15	2	Paranoid schizophrenia	Chronic bronchitis
26	M	39	131	14	..	64	130	96	62	72	100	—31; —8	7.6	6.8	14	11	3	Paranoid schizophrenia	Normal
27	F	38	139	18	..	86	120	80	84	98	80	....	6.6	6.6	16	13	3	Paranoid schizophrenia	Normal
28	F	33	152	9	..	84	130	70	84	96	80	—20	7.6	6.0	12	9	3	Paranoid schizophrenia	Blurred disks plus exudate
29	F	42	101	..	3	96	148	70	88	116	95	— 4	6.6	...	13	..	..	Paranoid schizophrenia	Fibroid uterus
30	F	51	107	1	6	72	140	70	72	120	75	....	6.8	...	16	..	..	Paranoid schizophrenia	Normal
31	M	38	149	5	..	60	117	72	78	102	80	....	9.0	...	17	..	..	Paranoid schizophrenia	Normal
32	M	21	152	..	1	78	120	60	66	100	90	....	8.0	7.0	17	11	6	Schizophrenia	Normal
33	M	25	135	7	..	66	115	50	70	76	80	....	7.4	6.6	16	12	4	Paranoid schizophrenia	Normal
34	F	48	145	..	3	90	140	70	84	98	80	....	5.8	5.8	12	9	3	Paranoid schizophrenia	Normal
35	F	35	92	4	..	88	124	86	80	104	75	....	5.0	4.4	14	10	4	Catatonic schizophrenia	Normal
36	M	28	115	5	..	66	110	70	72	104	90	....	8.0	7.2	14	9	5	Schizophrenia	Normal
37	F	34	85	7	..	80	96	60	90	180	90	....	5.4	5.0	15	10	5	Paranoid schizophrenia	Normal
38	M	17	120	1	6	92	140	65	..	...	95	—11	6.6	...	11	..	..	Schizophrenia	Normal
39	F	35	92	1	..	64	95	65	80	120	100	—12	6.8	6.0	20	12	8	Paranoid schizophrenia	Normal
40	F	20	128	..	¼	72	110	68	100	108	70	—15	5.4	6.4	19	10	9	Catatonic schizophrenia	Normal
41	F	36	90	17	..	80	104	66	90	140	..	....	8.0	7.0	16	10	6	Hebephrenic schizophrenia	Normal
42	M	38	151	18	..	84	130	75	84	100	85	....	7.6	...	12	..	..	Hebephrenic schizophrenia	Normal
43	F	61	...	32	..	..	170	90	100	136	75	....	6.4	...	14	..	..	Schizophrenia	Normal
44	F	75	...	35	..	62	190	90	84	120	75	....	7.0	...	14	..	..	Catatonic schizophrenia	Normal
45	F	57	130	20	..	76	140	90	76	92	90	....	6.4	...	16	..	..	Paranoid schizophrenia	Chronic pulmnary disease
46	M	49	...	27	..	72	142	88	72	86	80	....	7.6	7.0	14	11	3	Catatonic schizophrenia	Normal
47	F	68	...	21	..	104	210	110	96	116	90	....	6.0	5.6	11	9	2	Paranoid schizophrenia	Diabetes mellitus
48	F	47	160	24	..	120	220	110	120	156	85	....	6.4	...	11	..	..	Paranoid schizophrenia	Hypertension; diabetes mellitus
49	F	58	121	28	..	78	138	92	78	132	64	....	9.2	7.6	16	10	6	Catatonic schizophrenia	Normal
50	F	39	126	10	..	100	130	90	100	120	90	....	6.8	6.2	11	8	3	Hebephrenic schizophrenia	Normal
51	F	56	168	35	..	78	230	110	78	96	75	....	...	7.0	..	11	..	Catatonic schizophrenia	Hypertension
52	F	43	118	2	..	84	144	80	100	124	85	....	8.0	...	13	..	..	Catatonic schizophrenia	Normal
53	F	66	...	46	..	92	144	80	120	...	70	....	6.6	...	18	..	..	Catatonic schizophrenia	Normal
54	F	66	...	46	..	120	220	110	108	116	85	....	6.8	...	15	..	..	Catatonic schizophrenia	Normal
55	F	45	126	17	..	144	134	80	128	160	90	....	7.2	...	11	..	..	Paranoid schizophrenia	Normal
56	M	..	...	..	..	52	100	60	52	66	70	....	8.2	...	20	..	..	Schizophrenia	Normal

gave a value somewhat greater. However, when the radioactive method was used the pathway was longer, being from arm to arm and from the jugular vein to the arm.

DATA

A complete summary of all our data is presented in table 2.

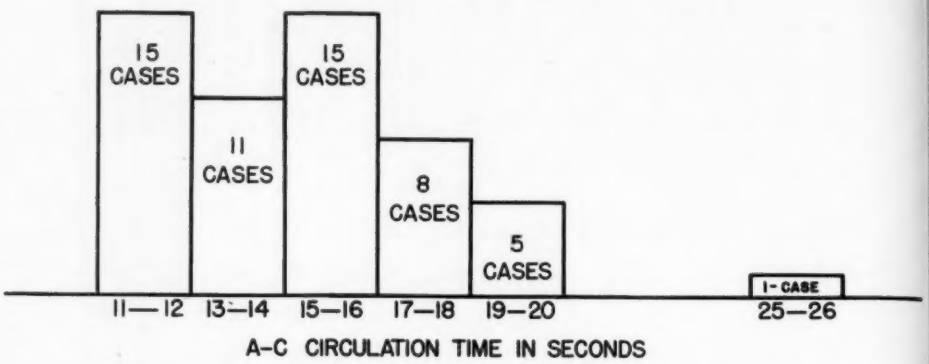

Chart 1.—Graph for the arm to carotid circulation time, expressed in seconds, in fifty-five patients with schizophrenia.

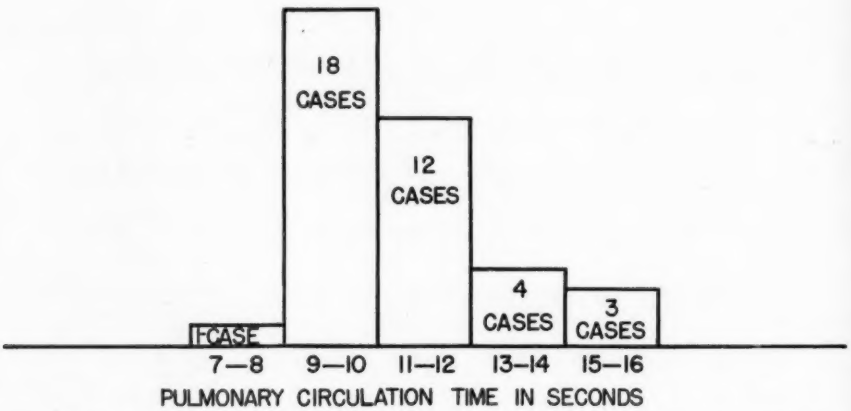

Chart 2.—Graph for the crude pulmonary circulation time, expressed in seconds, in thirty-eight patients with schizophrenia.

Fifty-six patients (twenty-two males and thirty-four females) were studied, all of whom had a condition diagnosed as schizophrenia. Patients for whom the diagnosis was doubtful were excluded from this series. The average age was 39.7 years, and the range in age was from 15 to 75 years. The average weight of the patients was 128.9 pounds (58.1 Kg.); the range was from 80 to 200 pounds (36.3 to 90.7 Kg.). The duration of the illness as determined from the hospital records

averaged nine years, the range being from one week to forty-six years. The pulse rate as determined by counting the pulse during basal conditions before the test averaged 81.9 beats per minute, the range being from 42 to 144 beats. The systolic blood pressure as taken by a sphygmomanometer averaged 131.1 mm. of mercury; the range was from 90 to 220 mm. The diastolic blood pressure averaged 75.8 mm. of mercury, the range being from 64 to 110 mm. The percentage of hemoglobin, as determined in most cases by the Tallqvist method, averaged 80.5, the range being from 70 to 100 per cent. The basal metabolic rate, determined for only sixteen of these patients, averaged —9 per cent, the range being from +30 to —31 per cent.

The arm to carotid circulation time was determined in fifty-five patients. The average arm to carotid circulation time was 14.9 seconds,

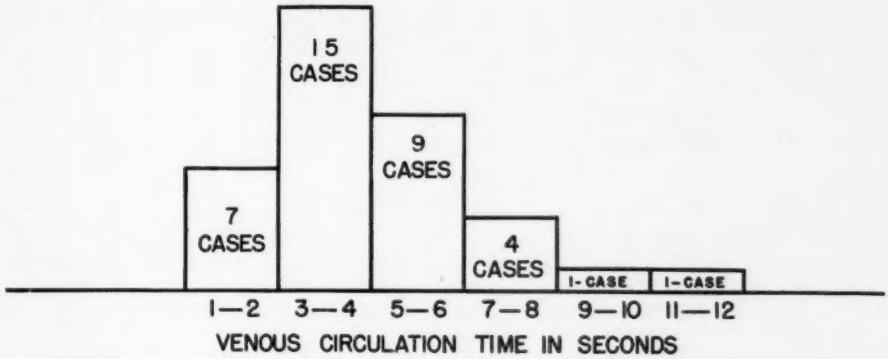

Chart 3.—Graph for the venous circulation time, expressed in seconds, in thirty-seven patients with schizophrenia.

the range being from 11 to 26 seconds. The crude pulmonary circulation time was determined in thirty-eight patients. The average crude pulmonary circulation time was 10.8 seconds, the range being from 9 to 16 seconds. The venous circulation time was calculated in thirty-seven cases. The average venous circulation time was 4.4 seconds, with a range from 2 to 11 seconds. The optimal dose of sodium cyanide used in determining the arm to carotid circulation time averaged 6.8 mg. (0.116 mg. per kilogram of body weight), the range being from 5 to 9.2 mg. The average dose of sodium cyanide used in determining the crude pulmonary circulation time was 6.15 mg., with a range of from 4.4 to 7.6 mg. When sodium cyanide was administered as a 2 per cent solution, the average amount injected in determination of the arm to carotid circulation time was 0.34 cc., and the average volume used for the crude pulmonary circulation time was 0.308 cc.

Determinations of the circulation time were repeated on different days on patients 40, 1 and 22. The results of these tests are presented in table 3. It is of interest that in patient 40 on whom seven determinations were made under basal conditions within a period of about ten weeks, the arm to carotid circulation time varied from 19 to 10.5

TABLE 3.—*Repeated Determinations of Circulation Time for Three Patients with Schizophrenia*

Case	Sex	Age, Yr.	Weight, Lb.	Known Duration of Disease	Date of Test	Pulse Rate During Fasting	Arterial Blood Pressure, Mm. Mercury		Pulse Rate During Test		Dose Sodium Cyanide, Mg.		Circulation Time, Sec.		
							Systolic	Diastolic	Initial	Maximum	Arm to Carotid	Pulmonary	Arm to Carotid	Pulmonary	Venous
40	F	20	128	1 wk.	8/29/35	72	110	68	80	120	5.4	6.4	19	10	9
					9/ 1/35	68	110	60	68	92	7.0	6.6	14	11	3
					9/14/35	68	110	70	72	96	7.4	6.6	14	10	4
				(nonbasal)	9/14/35	72	110	74	72	126	7.8	6.6	14	10	4
					10/ 1/35	76	120	70	76	100	7.0	6.0	11	9	2
					10/ 5/35	76	117	64	96	112	7.4	6.4	11	10	1
					10/24/35	..	...	..	80	110	7.4	...	13	..	..
					11/10/35	..	...	..	120	128	...	...	13	..	..
1	M	21	127	5 yr.	3/26/35	84	110	84	..	...	6.4	5.2	18	11	7
					3/ 8/35	..	...	..	..	...	8.0	6.0	18	10	8
					7/16/35	72	120	70	..	...	1.8	6.0	14	11	3
22	M	49	200	3 yr.	7/ 4/35	44	105	60	48	60	8.0	7.6	18	17	1
					7/ 5/35	48	90	55	44	60	8.0	7.6	18	16	2

TABLE 4.—*Constants for Distributions of Determinations of Circulation Time*

	No. of Patients	Minimum Value	Maximum Value	Range	Mean	Standard Deviation	Coefficient of Variation, %
Arm to carotid.....	55	11	26	15	15.0 ± 0.28	3.1 ± 0.30	20.6
Crude pulmonary.....	38	9	16	7	10.8 ± 0.21	1.9 ± 0.22	17.6
Venous.....	37	2	11	9	4.4 ± 0.24	2.2 ± 0.51	50.1

TABLE 5.—*Correlations Between Pulse Rate During Fasting and Circulation Time*

	Coefficient of Correlation	Probable Error
Pulse rate during fasting vs. arm to carotid circulation time...	—0.60	± 0.08
Pulse rate during fasting vs. crude pulmonary circulation time.	—0.70	± 0.06
Pulse rate during fasting vs. venous circulation time.....	—0.27	± 0.07

seconds, the crude pulmonary circulation time remained fairly constant and the venous circulation time decreased. During this time the patient became increasingly agitated. In patient 1 there was also a decrease in the arm to carotid circulation time, of from 18 to 14 seconds, and a decrease in the venous circulation time. In the third patient there was little difference in the determinations.

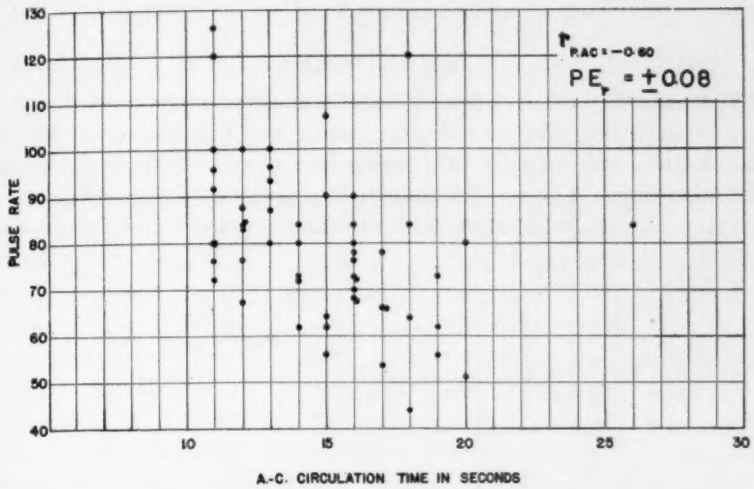

Chart 4.—Correlation between the pulse rate during fasting and the arm to carotid circulation time in fifty-three patients with schizophrenia. The coefficient of correlation is —0.60; the probable error is ±0.08.

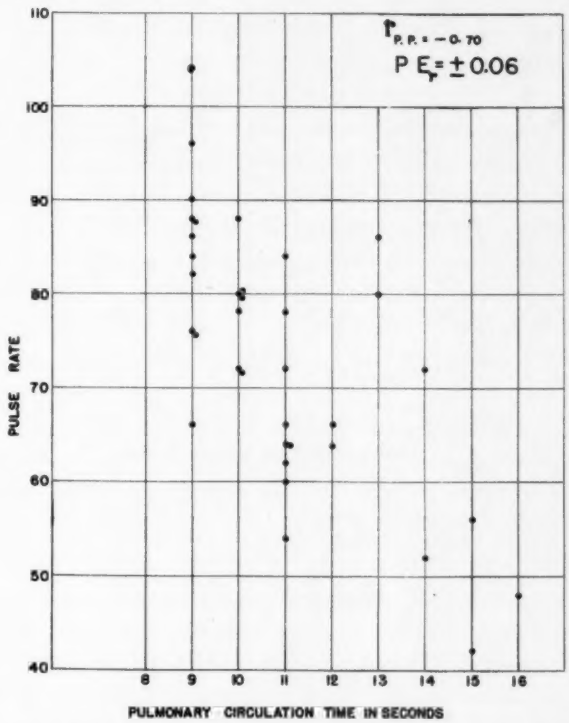

Chart 5.—Correlation between the pulse rate during fasting and the crude pulmonary circulation time in thirty-eight patients with schizophrenia. The coefficient of correlation is —0.70; the probable error is ±0.06.

CORRELATIONS

With the method of Bravais, significant correlations were found to exist between the pulse rate during fasting and the arm to carotid circulation time, and the pulse rate during fasting and the crude pulmonary circulation time. The coefficients of correlation and the probable errors are given in table 4. The individual values for these determinations are

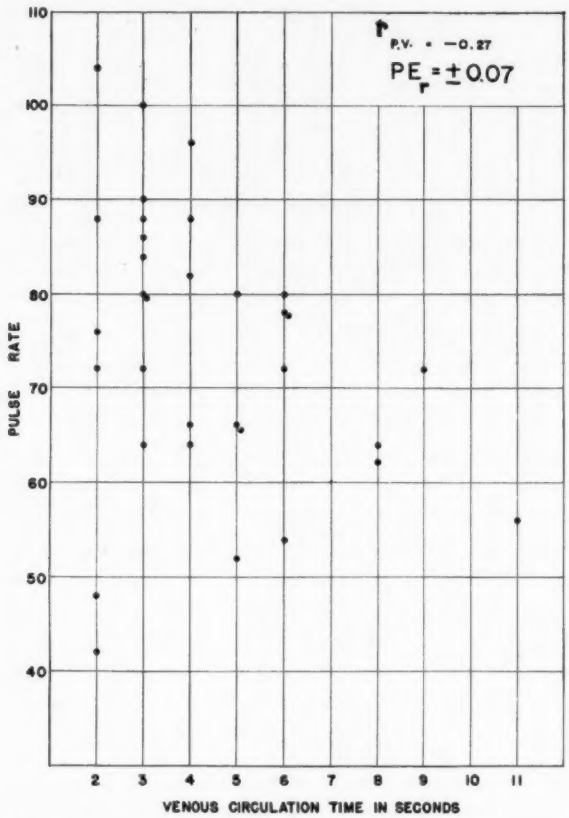

Chart 6.—Correlation between the pulse rate during fasting and the venous circulation time in thirty-seven patients with schizophrenia. The coefficient of correlation is —0.27, and the probable error is ±0.07.

plotted in charts 4, 5 and 6. With a simpler method, lack of correlation was found to exist between the age and the duration of disease, the systolic and the diastolic blood pressure and the arm to carotid, the crude pulmonary and the venous circulation time. There was not a sufficiently large number of determinations of the basal metabolic rate to make any correlation of value. The hemoglobin values were usually determined by the Tallqvist method, and since this method gives a rough

approximation of the hemoglobin value, it was thought that any correlation between the value for hemoglobin and the circulation time would not be reliable.

COMMENT

The data presented demonstrate that the average circulation time, as determined by the sodium cyanide method in this series of fifty-six patients with schizophrenia, is within the same limits as that found for normal persons. This holds true for all the patients, except patient 6. In determining the velocity of the blood flow in normal subjects by the sodium cyanide method, three authors reported average values of 15.6, 15.6 and 15.7 seconds, respectively, for the arm to carotid circulation time. The values for the arm to carotid circulation time for normal persons used as controls reported by Freeman,[4] however, were greater, being 21.9 seconds.

In this study the average arm to carotid time for patients with schizophrenia was 14.9 seconds, which closely approximates the normal value. The average value for the crude pulmonary circulation time in patients with schizophrenia was about the same as that reported by Robb and Weiss [2] for their series of normal subjects. It is also of interest to note the similarity in the distribution curve shown in chart 1 in our study and that in figure 2 in the article by Robb and Weiss.[2]

Freeman reported a greater value for the arm to carotid circulation time in two series of patients with schizophrenia, the average being 25.55 ± 0.77 for the first series and 27.94 ± 1.22 for the second. In another series of determinations of the arm to carotid circulation time for patients with schizophrenia during nonbasal conditions, an average value of 23.01 ± 0.79 seconds was reported. Only determinations during basal conditions were made in our study, and hence our data throw no light on the comparative circulation times of patients during basal and nonbasal conditions.

Since the complete data on Freeman's observations were not presented, it is difficult to explain his results. The mean pulse rate reported for his series was 58 beats per minute. The mean pulse rate during fasting in this series averaged 82 beats per minute. This difference in the pulse rate might contribute toward explaining the differences between the values for the circulation time given by Freeman [4] and those reported in this study, since there is a negative correlation between the pulse rate and the circulation time.

These results agree with those obtained by Freeman in indicating a lack of correlation between the circulation time, the age and the systolic and diastolic blood pressure.

CONCLUSIONS

In a series of determinations by the sodium cyanide method on fifty-five patients with schizophrenia, the average arm to carotid circulation time was 14.9 seconds, the range being from 11 to 26 seconds. These values are within normal limits.

In a series of determinations by the sodium cyanide method on thirty-eight patients with schizophrenia, the average crude pulmonary circulation time was 10.8 seconds, the range being from 9 to 16 seconds. These values are within normal limits.

In a series of thirty-seven patients with schizophrenia the average venous circulation time was calculated from the values for the arm to carotid circulation time and the crude pulmonary circulation time, as determined by the sodium cyanide method. The average venous circulation time was 4.4 seconds, the range being from 2 to 11 seconds. These values are within normal limits.

This study does not corroborate the conclusion of Freeman [4] "that schizophrenia is characterized by an abnormal slowing of the circulation time."

Prof. C. MacFie Campbell, of the Boston Psychopathic Hospital, Dr. Kenneth J. Tillotson, of the McLean Hospital, and Prof. E. B. Wilson, statistician of the Harvard University School of Public Health, cooperated in this study.

STUDIES IN DISEASES OF MUSCLE

II. EFFECT OF VARYING AMOUNTS OF INGESTED CREATINE ON CREATINE TOLERANCE IN PROGRESSIVE MUSCULAR DYSTROPHY

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In a previous report [1] we discussed various factors influencing the ability of patients with progressive muscular dystrophy to retain ingested creatine. In the series of twenty cases investigated the creatine tolerance was impaired so that a large part of an administered dose of creatine was excreted unchanged in the urine. The defect in the ability to retain exogenous creatine varied with the degree of muscular disability. In adult patients in the early stages of the disease as much as 82 per cent of the ingested creatine was retained, whereas in patients showing advanced muscular wasting the creatine tolerance was impaired to the extent that all the ingested dose of creatine was excreted unchanged.

The amount of creatine usually administered in performing the creatine tolerance tests in our studies was 1.32 Gm. However, other workers have used widely different amounts. Thus, Boothby and his associates [2] gave 1 Gm.; one of us (A. T. M.),[3] 2.73 Gm.; Harris and Brand,[4] 0.5 Gm., and Cuthbertson and Maclachlan,[5] 4.4 Gm. The

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From the New York Hospital and the Department of Medicine, the Cornell University Medical College, and the Russell Sage Institute of Pathology.

1. Milhorat, A. T., and Wolff, H. G.: Studies in Diseases of Muscle: I. Metabolism of Creatine and Creatinine in Progressive Muscular Dystrophy, Arch. Neurol. & Psychiat. **38**:992 (Nov.) 1937.

2. Boothby, W. M.; Adams, M.; Power, M. H.; Edgeworth, H.; Moersch, E. P.; Woltman, H. W., and Wilder, R. M.: Myasthenia Gravis: Second Report on the Effect of Treatment with Glycine, Proc. Staff Meet., Mayo Clin. **7**:737, 1932.

3. Milhorat, A. T.: Ueber die Behandlung der progressiven Muskeldystrophie, und ähnlicher Muskelerkrankungen mit Glykokoll, Deutsches Arch. f. klin. Med. **174**:487, 1933.

4. Harris, M. M., and Brand, E.: Metabolic and Therapeutic Studies in the Myopathies, with Special Reference to Glycine Administration, J. A. M. A. **101**: 1047 (Sept. 30) 1933.

5. Cuthbertson, D. P., and Maclachlan, T. K.: The Treatment of Muscular Dystrophy with Glycine, Quart. J. Med. **3**:411, 1934.

results of these investigators were in agreement that in progressive muscular dystrophy there is impaired creatine tolerance. However, it is uncertain whether their findings can be compared quantitatively, as it is not known how the amount of creatine retained may vary when different amounts are administered. It is of interest, therefore, to know the effect of varying amounts of ingested creatine on the creatine tolerance. Such knowledge is significant not only for the practical performance of the test but for an understanding of the mechanism of creatine retention. In the present studies the effect of different amounts of administered creatine was determined.

METHODS

The subjects were four patients with progressive muscular dystrophy in whom the ability to retain ingested creatine was definitely impaired and one patient (A. C.) with muscular atrophy of the Charcot-Marie type who showed only a slight defect in the metabolism of creatine.

The patients were maintained on a diet free from creatinine and creatine, which was kept constant in amount and in its content of protein, carbohydrate and fat for the entire experimental period. The urine, carefully collected in twenty-four hour specimens, was analyzed daily for preformed creatinine, creatine and total nitrogen, according to the methods previously described.[1] The creatine was administered in a single dose on the first day of the experimental period.

OBSERVATIONS AND COMMENT

The data are shown in tables 1 and 2. All chemical determinations were made daily, but for the sake of brevity only the average daily values for the periods are given. It will be seen from the data that when exogenous creatine is offered the organism, the absolute amount retained is not fixed but is dependent on the amount of creatine administered. Within fairly wide limits the percentage retention is constant. For example, when varying amounts of creatine (from 0.66 to more than 5 Gm.) were administered to patient M. S., the percentage retention was unchanged. The absolute amounts retained, on the other hand, were increased from 0.21 Gm., when 0.66 Gm. was administered, to 1.28 Gm., when 5.28 Gm. was given. Only when very large amounts of creatine were ingested was the amount retained no longer proportional to that administered. Thus, when increasingly large amounts (5.28, 6.6 and 7.92 Gm.) were given, the absolute amount retained was constant (about 1.2 Gm.). The percentage retention decreased with increasing amounts of ingested creatine. Apparently, the amount retained under these conditions represents the maximum ability of the organism to hold exogenous creatine. These findings indicate that the retention of moderate amounts of exogenous creatine is a function of

TABLE 1.—*Effect of Varying Amounts of Ingested Creatine on Creatine Tolerance* *

Patient	Days in Period	Total Urinary Nitrogen Daily, Gm.	Urinary Preformed Creatinine Daily, Gm.	Urinary Creatine as Creatinine Daily, Gm.	Creatine		
					Ingested, Gm.†	Retained, Gm.‡	Retained, Percentage
M. S.	3	5.94	0.655	0.196			
F	2	6.66	0.633	0.548	1.32	0.346	29.7
51.2 Kg.	1	6.61	0.670	0.318			
18 yr.	2	6.39	0.693	0.996	2.64	0.749	29.9
	2	6.84	0.716	0.270			
	2	6.81	0.735	1.471	3.96	0.869	25.0
	3	6.65	0.667	0.362			
	2	6.67	0.683	1.796	5.28	1.276	27.5
	3	5.78	0.682	0.312			
	3	6.40	0.696	1.958	7.92	1.232	17.7
	2	5.80	0.642	0.280			
	2	5.41	0.683	0.290			
	1	6.22	0.648	0.652	0.66	0.210	27.6
	2	5.83	0.668	0.241			
	2	5.86	0.678	2.225	6.60	1.200	20.7
	2	6.02	0.630	0.274			

* The creatine was ingested on the first day of the periods indicated. One dose only was given.
† Expressed as crystalline creatine (containing 1 molecule of water).
‡ Expressed as water-free creatine.

TABLE 2.—*Effect of Varying Amounts of Ingested Creatine on Creatine Tolerance*

Patient	Days in Period	Total Urinary Nitrogen Daily, Gm.	Urinary Preformed Creatinine Daily, Gm.	Urinary Creatine as Creatinine Daily, Gm.	Creatine*		
					Given per Os (Crystalline), Gm.	Retained (Water-Free), Gm.	Retained, Percentage
W. K.	3	8.54	0.919	0.378			
M	2	8.51	0.978	0.771	1.32	0.248	21.4
61 Kg.	1	8.35	0.885	0.451			
17 yr.	2	9.10	0.860	1.945	5.00	0.853	20.9
L. V.	4	5.52	0.257	0.578			
F	2	5.91	0.264	1.021	1.32	0.132	11.4
50.7 Kg.	6	6.80	0.254	0.571			
27 yr.	2	7.44	0.298	2.227	5.00	0.738	12.6
T. P.	3	5.08	0.251	0.457			
F	2	5.72	0.264	0.876	1.32	0.186	16.2
43.7 Kg.	2	6.46	0.307	0.673			
13 yr.	2	6.58	0.369	2.136	5.00	0.920	21.2
A. C.	4	9.43	1.851	0.007			
M	2	8.36	1.863	0.108	1.32	0.926	79.8
67 Kg.	1	10.75	2.028	0.050			
26 yr.	1	9.38	2.001	1.679	5.00	2.435	57.2
	1	6.86	1.800	0.042			

* Creatine as purchased (air-dried crystals) contains 1 molecule of water. Therefore, 1.32 Gm. creatine (with 1 molecule of water) = 1.16 Gm. creatine (water-free) = 1 Gm. creatinine; 5 Gm. creatine (with 1 molecule of water) = 4.31 Gm. creatine (water-free) = 3.788 Gm. creatinine.

the amount offered the organism, even in subjects with lowered tolerance. It appears likely from the work of Folin [6] and Chanutin [7] that this is not due to any change in alimentary absorption. Folin was unable to find any trace of creatine in the feces after feeding creatine, and Chanutin found its absorption to be complete. Rose and Dimmitt [8] could find no evidence of its destruction in the alimentary tract. Furthermore, the excretion in the urine of the entire amount of ingested creatine in some patients with seriously impaired creatine tolerance gives further evidence that all the creatine is absorbed from the intestine. Thus, in patient G. G. (Milhorat [3]) 2.62 Gm. of creatine administered each day for three days was eliminated quantitatively in the urine. In other cases to be reported in a later paper, 1.32 Gm. of creatine was completely excreted.

This finding that the percentage retention of creatine is a constant within rather wide limits is of further significance. The creatine tolerance of patients as determined by different investigators can be compared directly, even when the amounts of creatine administered were different. The optimal amount of creatine used in performing the creatine tolerance test is probably 1.32 Gm. This amount of creatine (crystalline) is equivalent to 1.0 Gm. of creatinine. Since the urinary creatine is determined as creatinine, the percentage retention is readily computed. The use of smaller amounts may yield less accurate results because the daily variations in the spontaneous output of creatine will represent a greater source of error than when larger amounts are given. Amounts larger than 1.32 or 2.64 Gm. are unnecessary. Obviously, doses so large that the constancy of the percentage of creatine tolerance no longer holds are to be avoided, unless the maximum absolute retention is to be determined.

CONCLUSIONS

When creatine is ingested, the absolute amount retained is not fixed but is relative and dependent on the amount, within fairly wide limits, of creatine administered. The percentage retention, however, is constant. Only when very large amounts are ingested is the amount retained no longer proportional to the amount administered. In these instances, the absolute amounts retained are constant and apparently represent the maximum capacity of the body to hold exogenous creatine.

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6. Folin, O.: The Chemistry and Bio-Chemistry of Kreatin and Kreatinin, Festskrift tillegnad Olof Hammarsten, Uppsala, C. J. Lundström, 1906, pt. 3, p. 1.

7. Chanutin, A.: The Fate of Creatine When Administered to Man, J. Biol. Chem. **67**:29, 1926.

8. Rose, W. C., and Dimmitt, F. W.: Experimental Studies on Creatine and Creatinine: VII. The Fate of Creatine and Creatinine When Administered to Man, J. Biol. Chem. **26**:345, 1916.

ENOSTOSES OF THE CALVARIUM

INCIDENCE AT AUTOPSIES IN STATE HOSPITALS *

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Since 1907 observations at autopsy of a thickened, rugose inner table in the frontal region of the calvarium has been to me a persistent challenge. There seemed to be no tradition concerning enostoses in the calvarium and no correlation with clinical observations. When the articles by Moore [1] and Carr [2] came to hand, nearly twenty-nine years later, I reviewed the protocols in the pathologic laboratory of the Massachusetts Department of Mental Diseases for the number of cases of enostoses of the inner table of the skull in that investigative service and found in the 3,250 records an incidence of 230, or 7 per cent. These changes, when extreme, consisted of irregular rolls of bony tissue, converging toward the nasal end of the (present or obliterated (metopic) suture. For the most part these bony masses were irregular and dense, the diploe being converted into tissue of ivory-like firmness. Now and then they had a less condensed appearance and were porous, with diploe; more often than not, the dura mater was adherent in this region (fig. 1); in fact, a greater part of this membrane had literally been absorbed, and what remnants were visible had a thin, stretched, ribbon-like or shredded appearance, unlike that over the vertex and parietal regions, where the dura might be thick and even adherent but not reduced, absorbed or shredded.

Yolton [3] reviewed many articles written in the last ninety years and published the description, with a picture, of 4 specimens in the Museum of the Norman Bridge Laboratory of Pathology, at the Rush Medical College.

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* A review of 3,250 autopsies in the Massachusetts state hospitals for mental disease and defect.

1. Moore, Sherwood: Calvarial Hyperostosis and the Accompanying Symptom Complex, Arch. Neurol. & Psychiat. **35**:975 (May) 1936.

2. Carr, Archie D.: Neuropsychiatric Syndromes Associated with Hyperostosis Frontalis Interna: Preliminary Report, Arch. Neurol. & Psychiat. **35**:982 (May) 1936.

3. Yolton, L. W.: Ventral Symmetric Hyperostoses of the Inner Table of the Calvarium, Tr. Chicago Path. Soc. **13**:181, 1928-1931.

In an authoritative paper, Greig [4] reported on 188 skulls in the Museum of the Royal College of Surgeons, Edinburgh, in 32 of which, or 17.2 per cent, osteophytes occurred. He had no hesitancy in relegating many previously published ideas to the discard. He expressed the belief that the nodular masses come from the bone and not from the dura and that the transition from the bone to the osteophyte is

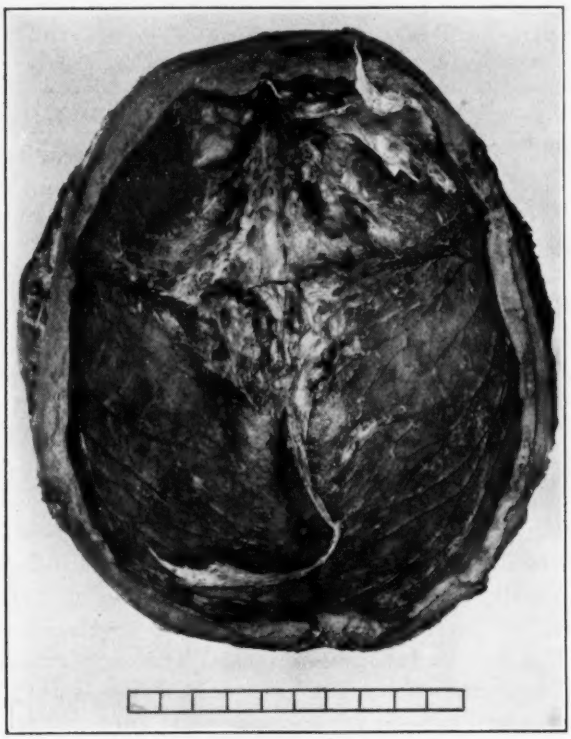

Fig. 1.—Photograph of the calvarium of a feebleminded woman aged 63, who had been under state care for forty years. The body was 160 cm. in length and weighed 200 pounds (45.4 Kg.). The calvarium was heavy—weight, 470 Gm.—and the whole inner table was thickened (hyperostosis), with focal elevations on the frontal bone (enostosis). Note the shredded appearance of the adherent dura. (This specimen was brought in by Dr. P. I. Yakovlev, Waltham, Mass., after the series had been completed, and therefore is not one of the series of 230.

abrupt, space for pacchionian granulations always being provided. Four of the skulls were of men and 28 of women; 2 only were obtained from patients with mental disease. Two of the patients were fat; 5

4. Greig, D. M.: On Intracranial Osteophytes, Edinburgh M. J. **35**:165 (April); 237 (May) 1928.

had other bony changes; 5 died of malignant disease, and 3 had arthritis, but no other lesion consistently accompanied the thickenings of the skull. Greig pointed out that the diploe has not the same function as the marrow of long bones, which builds for locomotion, whereas the skull protects only and does not repair fractures and defects. A large section of the monograph is taken up with the classification of the words used to describe this appearance, and Greig quoted and criticized Rokitansky and Lobstein as to their terminology and data on age, pregnancy, etc. He expressed his agreement that pregnancy is the cause of the nodular type, though he described a case in which a skull, with thin plaques of bone over the inner surface, from a woman who had recently been delivered had come to his museum. He discarded the theory of association with syphilis, mental disease or the puerperal state. He expressed the opinion that the skeleton gives off bone which is absorbed and redeposited.

Stewart [5] reviewed several English contributions to the subject of local thickenings of the frontal bone; all but one of his citations dealt with cases of mental disease, but in no instance was a large number reported. Stewart reported on 5 patients he had seen in fifteen years; they were fat and had been in a hospital for mental disease for several years. The average weight of the brains was under 1,300 Gm. The pituitary gland, which was examined in 3 cases, showed fibrosis of the anterior lobe. Stewart concluded that he was dealing with a hitherto undifferentiated type of dyspituitarism.

Bullen,[6] in a summary of 1,565 postmortem examinations, representing the largest series of cases of mental illness heretofore reported in which enostoses is considered, found the condition in 1 per cent.

Freeman,[7] in a personal communication, gave me the number of cases of enostoses of the calvarium (24, or 1.51 per cent) observed at 1,514 autopsies performed at the Worcester State Hospital. His figures agreed with those of Bullen.

Dupré's [8] account was the first of its kind and is quoted verbatim because of the picturesque description of the inner surface of the calvarium. The case was not considered one of uncomplicated enostoses, but the duration of symptoms, treatment and observations at autopsy are given.

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5. Stewart, R. M.: Localized Cranial Hyperostosis in the Insane, J. Neurol. & Psychopath. **8**:321 (April) 1928.

6. Bullen, F. St. John: Abstract of 1565 Postmortem Examinations Performed at Wakefield Asylum, J. Ment. Sc. **36**:15 (Jan.) 1890.

7. Freeman, William: Personal communication to the author.

8. Dupré, M.: Bony Excrescences on a Human Skull, Phil. Tr., London **3**:295, 1700.

Nicholas Brodes of 30 Years of Age, having been afflicted for the space of ten years with an incessant headache, which for the last 12 months before his Decease had been more violent than formerly and deprived him of his sight, upon the 15th of March 1697, was received into the Hotel Dieu. After his head was shaved, there appeared a large tumor which extended itself over the Hairy Scalp. In the midst of the left parietal-bone there was a pulsation of an artery and a small fluctuation, the rest of the tumor being exceedingly hard. M. Dupré fearing this might be an aneurysm was unwilling to open the tumor till he was constrained to it by the Importunate Intreties of the patient who chose rather the Hazard of his Life than longer to endure so exquisite a Torment. As soon as an Aperture was made, there issued out a quantity of thick concreted Blood which wet the Bolsters at every Dressing. The 2nd day he felt a hard body with his probe, Loose in the Flesh which being taken out appeared to be a small fragment of a bone exfoliated, resembling a small Comb-Brush. Upon the 4th day the Patient Dy'd. In Dissecting the Head the Tumified part of the skull appeared to rise more than an inch above the sound bone. The whole swelling of the cranium was made up of several substances not unlike the little Horns or innumerable small Hollow Cones with their points downward; besides a great number of Bony Fibers, straight stiff and pointed resembling the Teasels used by Cloth Workers.

In the next place there were several holes, some of which perforated the Skull, others not. There was no Distinction of the Sutures. The meninges were mortified and Confounded Together and in part adhered to the Bony Excrescences of the Left Parietal Bone; Nevertheless the Brain was sound and entire. The Inequalities of the inner Surface of the Cranium, resembled Melted Metall poured down from a considerable height, on a light moving sand; or the inside of a Grotto, in which the Stones get out in an irregular manner. The whole left side had lost its natural Figure, and the right had only a few Impressions, made by the beating of the arteries of the Dura Mater.

There was no appearance, on an exact search, of any Venereal Distemper to be found, whence the Excresciences might be expected to proceed. It is therefore probable that the Blood Vessels of the Diploe might be burst by some accidental Blow on the Head or, eroded by some Acidities of the Humours, and the Blood be extravisated [sic] in its Cells. This Stagnating, and by Degrees arriving to a very high degree of Corruption it is not much to be admired that the more Ponderous part (by its great Acidity) should dissolve the Contiguous Bone, and after it has penetrated that, by eroding such nice and sensible Membranes as the Pericranium and Dura Mater, cause exquisite Pain.

To explain these irregularities of the Skull it may be considered that its upper Plate is composed of Strata of Bony fibers, lying Parallel to each other, and an Arched Figure. Now when the Volatile Acid Sublimes, and dissolves one end of the Bony Fiber it must by its Elasticity Spring up and become Erect on the other. If more of those happen to have those ends which remain on the Cranium around one Point, they form the Small Cones above noted, by means of a Viscious Water which Cements them Together and fills up Their Intersticies. On the contrary if they start separately, they form a capillary appearance.

Workman [9] reported the first case in the United States and described the condition as an osseous growth in tabular form, 1½ by 1 inch (3.8

9. Workman, J.: Exostosis Within the Cranium, Am. J. Insan. **15**:150, 1858-1859.

by 2.54 cm.) within the dura and attached immediately above and posterior to the crista galli; it penetrated the cerebrum for some distance.

Schiff and Trelles [10] reviewed Morel's monograph, which dealt with the anatomicoclinico-etiologic and pathogenic aspects of "hyperostosis." He had examined the bone histologically and observed it to involve the inner table only; the lesion always occurred in the obese, was apt to be associated with signs of an infundibulotuberal lesion, headache and varied neuropsychiatric trends and was more frequent in women. Schiff and Tralles suggested that disturbed metabolism may be due to the effect on the posterior lobe of the pituitary and that local pull of the adherent dura in oblique and tangential lines may account for the deposit of bone in the inner table; a clinical case was cited in which symptoms followed an injury to the head.

Four papers were written on this subject in the eighteenth century and fifty or more in the nineteenth, and already nearly ninety have appeared in the twentieth century. Do physicians today look more, think more or write more?

PERSONAL OBSERVATIONS

It is with the last group in the accompanying tabulation that this paper is chiefly concerned.

	No.
Protocols examined	3,250
Calvaria with general thickening	115
Calvaria with focal thickening	34
Calvaria with enostoses	230

Sex.—Persons of the two sexes were not attacked equally—49 were men and 181 women.

Age and Psychoses.—From the figures in table 1, it will be seen that there is a rise in incidence to 7.3 per cent in the decade of life from 21 to 30 years and again at the age of from 51 to 70 years, after which there is a sharp drop. This is hardly in accord with the figures in table 2, in which senile dementia is shown to be associated with enostoses in 10.1 per cent of the cases, and dementia praecox, in 8.8 per cent; this stresses age, on the one hand, and dementia on the other. Psychosis with cerebral arteriosclerosis, however, which may occur at about the same time in the patient's life as senile dementia is sixth in the list in respect to the frequency of association with enostoses, with an incidence of 6.2 per cent. On the basis of this table, the blunting process (i. e., dementia), whether early or late, seems to be associated with enostoses.

10. Schiff, P., and Trelles, J. O.: Syndrome de Stewart-Morel (hyperostose frontale interne avec adipose et troubles mentaux), d'origine traumatique, Encéphale **26**:768 (Dec.) 1931.

Body Length.—If one takes the average stature of men in the United States as 5 feet and 6 inches (167.5 cm.) and that of women as 5 feet and 3 inches (160 cm.), the height of the majority is at or under the minimum average (160 cm.). One must remember that the older the patient the shorter he is, on account of loss of elasticity in the intervertebral disks and spreading of the feet.

Nutrition.—Obesity having been reported as an associated finding by Moore [1] and Carr,[2] I noted carefully in descriptions of the external appearance the point

TABLE 1.—*Distribution of Patients with Enostosis on the Basis of Age*

Distribution According to Ages, Expressed in Decades, of 230 Patients with Enostosis		Percentage of Patients Showing Enostosis	Ages, Expressed in Decades, of Total Number of Patients (3,250) on Whom Autopsy Was Performed
Ages, Decades	Number of Patients		
0 - 10	1	2.43	41
11 - 20	3	4.0	74
21 - 30	13	7.3	178
31 - 40	17	4.1	412
41 - 50	26	4.5	568
51 - 60	45	7.4	608
61 - 70	52	7.9	655
71 - 80	48	1.02	468
81 - 90	17	0.87	195
91 -100	5	2.9	17
101 -110	0	...	1
Number of patients unknown	3	9.0	33
Total number of patients	230		3,250

TABLE 2.—*Relation of Psychoses to Enostosis in 3,250 Cases*

Psychoses	Patients with Enostoses		Total Number of Patients on Whom Autopsy Was Performed
	Number	Percentage	
Senile dementia	41	10.1	402
Dementia praecox	54	8.8	608
Epilepsy	14	7.8	178
Feeblemindedness (all grades)	23	7.7	296
Manic-depressive psychosis	18	7.1	251
Psychosis with cerebral arteriosclerosis	27	6.2	433
Alcoholism (all types)	11	5.9	185
All other psychoses	26	4.8	541
Dementia paralytica	16	4.4	356
	230		3,250

of the nutritional state; 17 persons were obese, but more than three times that number (53) were emaciated, with no postmortem evidence of having been of the fat type earlier in life, leaving the great majority (160) in the "fairly" or "poorly" nourished groups. An attempt was made to learn from an insurance company how many of the population are obese, but no figures are available. From observations at bathing beaches, railroad stations, public gatherings, hospitals, etc., this proportion—17 women, or about 7 per cent—seems high.

The liver was not weighed in each of the 230 cases under consideration, either because of the omissions that occasionally occur or because there were no scales, but in 105 cases the weight was 1,200 Gm. or below, with an average of 815 Gm.

One must consider, therefore, the factor of "nutrition," as mentioned by Robertson,[11] even though no histologic work was carried out on these livers.

Gallstones.—One would scarcely miss gallstones in examining a body post mortem; of the 230 cases of enostoses under consideration, gallstones were observed in 43, or in about one fifth, or 20 per cent. Osler and McCrae[12] mentioned that "some postmortem series show gallstones present in 25 per cent of women over 60 years of age."

Other Bony Changes.—In 55 cases there were observed skeletal fractures, exostoses, kyphosis or scoliosis and other changes, including arthritis. In 3 cases there was Paget's disease. This proportion of other bony changes seemed to have no significance. Advanced arthritis is not a common clinical finding in hospitals for mental disease. I have not often recognized it at the autopsy table if it was of minor grade.

TABLE 3.—*Distribution of Patients with Enostosis on the Basis of Body Length*

Body Length	Number of Patients
Patients not measured	5
Patients 150 cm. or under	51
Patients 160 cm.	100
Patients 170 cm.	57
Patients 180 cm.	16
Patients 190 cm.	1
	230

TABLE 4.—*Distribution of Patients with Enostosis on the Basis of Nutrition*

State of Nutrition	Number of Patients
Obese	17
Emaciated	53
Fairly or poorly nourished	160

Histopathologic Changes in the Pituitary Gland.—Since there has been a tendency to include changes in the pituitary as a possible source of stimulation to the growth of bone, the pituitary was examined in 20 patients showing enostoses who were not selected on the basis of nutrition or sex. The same criteria were used in each microscopic examination (that is, presence of membranes, condition of the sinusoids, proportion of the types of cells of the anterior lobe to each other, presence of fibrosis and presence or absence of invasive cells and dots of secretion in the posterior lobe).

In 13 cases the chromophobic cells were more numerous, but in only a few instances was there overlapping with excess of either acidophilic or basophilic cells in the anterior lobe. In 7 cases the basophilic cells were increased, and in 7 the acidophilic cells. In 8 cases cells from the pars intermedia invaded the posterior lobe. Fibrosis was observed in the anterior lobe in 3 cases, but the patients were not obese, as Stewart[5] reported his to be in 3 of 5 cases. There was lack of constancy, therefore, in the analysis of microscopic changes.

11. Robertson, W. Ford: A Text Book of Pathology in Relation to Mental Diseases, Edinburgh, W. F. Clay, 1900.

12. Osler, W., and McCrae, T.: The Principles and Practice of Medicine, ed. 10, New York, D. Appleton and Company, 1925, p. 571.

Glandular Changes.—While I made no pretense of recording the finer observations that the endocrinologist would make in detecting glandular signs, certain gross changes were noted in 89 of the 230 cases. For the most part, these consisted of "hair on the lips or chin," coarseness of hair on the head, fulness of the eyebrows or items such as cystic thyroid, small adrenals, cupped pituitary gland, atrophic ovaries, and the like. In 1 or 2 instances more striking changes were seen. The histologic structure of the glands in these cases was not recorded.

The syndrome described by Stewart and Morel,[10] consisting of frontal hyperostosis with obesity and mental disturbances, was present in 17 instances, but the triad was incomplete in the other 213 cases.

Tumor of the Uterus and Ovarian Changes.—As a last stand in the hunt for reasons for the preponderance of enostosis in women, tumor of the uterus was considered as a possible, though obscure, factor. Only 39 patients with enostosis, or 12.6 per cent, had a uterine tumor of any sort; so this, too, was given up as a possible concomitant condition.

One inquires naturally concerning the ovaries. In the notes the ovaries were recorded as atrophic, fibrosed, cystic, adherent or absent (probably removed because they were cystic), and there was tumor of one ovary in 121 of the 181 women. The ovaries were considered normal in 17 cases; no conclusion was drawn in 43 cases. These proportions could so well be distributed over the rest of the age groups (table 1) that I am not impressed with the significance of the changes.

Atrophy of the Brain.—Atrophy of the brain occurred in the frontal region, where enostoses occur, in 74, or roughly one third, of the cases.

Syphilis.—In the series there were 16 cases of dementia paralytica. In a few others there was a positive colloidal gold reaction of the spinal fluid, but even when these bits of evidence are added, syphilis does not have a commanding position in causation, as viewed post mortem.

Another chronic infection, tuberculosis, was less frequent than syphilis in this group, though it is often associated with deposit of calcium.

Trauma.—If enostosis were chargeable to trauma, it would, in all probability, be more common in men, though hardly in this location, and would be expected to be unilateral; there might be evidence of slight or massive subdural hemorrhage, but this was not the cause of death in any of the men in this series.

Race.—Eight of the 181 women and 1 of the 49 men—a total of 9 persons—were Negroes; statistics on other races indicated by name only are misleading, on account of marriage among the women or mixtures of races in the parents.

Duration of Mental Symptoms.—The duration of mental disease in these patients varied from a few days in the hospital to many years; roughly, a third had been known to be mentally diseased for less than five years, and two-thirds, for from five to fifty years. No significant relationship was observed.

Headache.—Headache was noted in the records of 17 patients, 13 of whom were women. A note usually specified that it occurred "during periods" or "since injury" or was of a "bilious" type. As a rule, few patients in hospitals for mental disease suffer from headache; indeed, the registration of physical distress in any form is below the expectation and often delays the detection of systemic disease.

Enostoses in Association with Intracranial Growths.—Since neurosurgeons take particular note of a localized bony growth in the skull as a guide to a more deeply placed tumor and in view of Cushing's observation that in 25 per cent of cases of meningioma in his series the tumor was so announced, it is of interest that in 9 (3.86 per cent) of this series of 230 cases of enostoses there was an intracranial tumor. In 5 cases the tumor was of the glioma type and involved areas

near the base, and in 4, it was a meningioma. In 1 case of the latter type the growth was at the base (with psammoma bodies) and pressed into the brain, producing hydrocephalus. In the other 3 cases the tumor was near the vertex; in 1 a focal enostosis lay over it and in the others the lesion was not so focalized.

Hypertension and Nephritis.—Although records of blood pressure were not made for all the patients, more were registered as having a pressure below than above 160 systolic; only 7 patients had a blood pressure of 200 systolic.

The kidneys showed frequent involvement; in 195 of the 230 cases nephritis was recognized, mostly of the chronic, progressive type, but, again, this is a common postmortem observation in persons in the corresponding age periods.

Vascular Changes.—In a review of the protocols for notes on general and cerebral vascular changes which would present a trend, if any, of sclerosis in the body and the brain, the following data were obtained:

	No. of Cases
Sclerosis of vessels of the trunk—specifically, the aorta and coronary arteries	163
Sclerosis of cerebral vessels—specifically, the basal arteries	112

The figures show that perhaps this change occurs in the greatest number of cases, but they are not reserved for this group; if sclerosis in general had any determinative bearing, one would observe enostosis in 77 per cent of the cases instead of 7 per cent. The tips of the terminal branches would be of greatest interest in this connection.

When the 230 cases of enostoses are divided on the basis of moderate and extreme severity, there were 139 instances of the first type and 91 of the second. Of the 91 cases in which the more striking grade of enostosis was shown, the ages of the patients were scattered from the second to the tenth decade of life; the number (87 cases) was most concentrated, however, from the fourth to the ninth decade, and in 24 of these cases (25 per cent), arteriosclerosis of the basal vessels was pronounced in from the seventh to the ninth decade.

In the 139 cases of moderate enostosis, the age in the majority of instances fell between the third and the ninth decade inclusive, and the number was concentrated in from the sixth to the ninth decade; of these arteriosclerosis of the basal vessels centered in from the seventh to the ninth decade in 30 cases, or 21.8 per cent. If the grade of enostoses is chargeable to advanced vascular change, the percentage in support is only 3.2.

COMMENT

The books on anatomy which were consulted agree that the calvarium is laid down as a membrane, while the base of the skull is originally cartilage; moreover, the outer table is nourished by the periosteum. The diploe, richly supplied with emissary veins, has its own arterial supply, while the inner table depends for nourishment on arterial twigs from the dura. Do these twigs become fibrosed in the frontal region after the period of growth, and does the inner table then receive a concessionary supply from the diploe? The irregularity of the corrugated appearance of the inner surface of the frontal bone would seem to show some vagary corresponding to that of vascular disease, long admitted to be unequal and beyond prediction. The explanations put forward by authors have a wide range: Yolton [3] quoted various

writers who advocated hypotheses involving factors ranging from the "recumbent position of the patients" [13] to the "compensatory deposit for atrophy of the brain." When there are so many opinions it is usually due to lack of satisfactory knowledge, and the same state is reflected in the present variety of views on the subject held by local pathologists. If, as Yolton [3] said, the lesions are "symptomless and are rarely diagnosed in life," there is no pressing reason for diagnosis and treatment; if, on the other hand, the case cited by Robertson [11] is indicative of what could happen, it may be well to be on the lookout. Robertson's book [11] has never been extensively quoted, though it deserves the highest praise. He observed thickening of the calvarium in 50 per cent of cases of mental disease in which autopsy was performed and osteosclerosis in 29 per cent and cited other authors freely. He mentioned the case of a woman in whom a growth of the inner table pressed on the brain. This point was again emphasized by Eisen,[14] who reported a clinical case in which there was evidence of increase in the bony deposit in thirteen months. Geschickter [15] referred to enostosis as a benign tumor which may project inward from the inner table of the anterior portion of the calvarium.

Some (Wolbach [16] and MacCallum [17]) observed this condition in parous women and considered it to be associated with altered calcium metabolism during pregnancy and, further, Wolbach [16] stated it to be a reaction to epidural hemorrhages occurring in labor. So it may; but in this series, however, two thirds of the women with enostoses had never been pregnant, and a fifth of the number with the condition were men.

Arteriosclerosis.—Although there is at present no proof that the dural vessels fibrose at their anterior extremity, one of the next histologic inquiries will be to compare the vascularity and state of the dural vessels in this portion of the skull with the condition in other regions. The blood vessels branching to supply the dura have no origin similar to those for the brain; theoretically, the anterior part of the dura should be well nourished, since it is supplied by twigs from the ethmoid branch of the ophthalmic artery and by the anterior branch of the middle meningeal artery, which comes from the internal maxillary artery and, thus, should resist untoward events.

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13. Dressler, L.: Ueber die Hyperostosen des Stirnbeins, Beitr. z. path. Anat. u. z. allg. Path. **78**:332 (Sept. 5) 1927.

14. Eisen, David: The Internal Frontal Hyperostosis Syndrome, Canad. M. A. J. **35**:24 (July) 1936.

15. Geschickter, Charles F.: Primary Tumors of Cranial Bones, Am. J. Cancer **26**:155 (Jan.) 1936.

16. Wolbach, S. B.: Personal communication to the author.

17. MacCallum, W. G.: A Text-Book of Pathology, ed. 3, Philadelphia, W. B. Saunders Company, 1924, p. 953.

It would be convenient to locate enostoses of the frontal bone if patients possessing the lesion in wards of hospitals for mental disease were all overweight, as a rapid survey might be made by means of roentgenography (fig. 2) and the symptoms observed for evidence of intracranial pressure, general or focal. The puzzle concerns the haphazard attack of calvarial enostoses on a stable group of the population whose daily life is more or less the same, with every one receiving the same food, and having the same sleeping hours and nearly all having

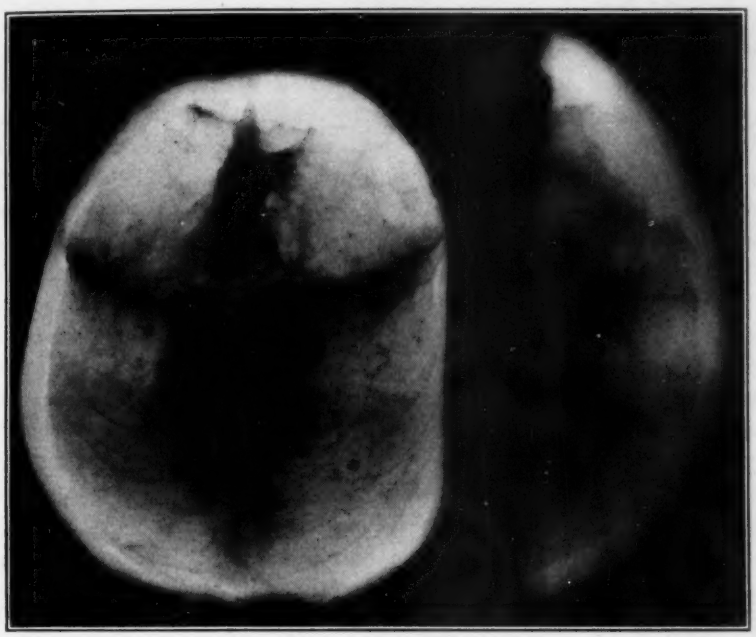

Fig. 2.—Roentgenogram (Dr. M. C. Sosman) of the calvarium illustrated in figure 1, showing the top and lateral views and demonstrating what may appear in the living subject. Note the general thickness of the calvarium and the wavy lines of thickening in both frontal bones, with a groove in the center for the longitudinal sinus, where there is no thickening. The appearance is characteristic of so-called "metabolic craniopathy."

the same recreation. It does not occur in patients who are chronically in bed, when gravity might exert a pull on the dural vessels in the anterior fossa (Dressler [13]) and thus stimulate proliferation of bone more in these patients than in others. Not in all cases, though in the majority, the dura mater is adherent to the enostoses.

I believe I can present a better name for the lesion than has hitherto been used; for purposes of clarity, I should employ "enostosis" as Dorland's "American Illustrated Medical Dictionary" defines it: "A

morbid growth developed within the cavity of a bone or within the cranium," omitting as confusing the terms hyperostosis, endostosis, osteophyte, osteoma, osteitis or exostosis, although under these various names the majority of previous articles have been written.

There is a higher incidence of enostosis (7 per cent) in this unselected series of 3,250 postmortem examinations in a psychiatric service than in any series reported to date. I believe that if every skull was weighed and measured and the dura removed from the inner table in every case in which it is adherent, even more examples would be found in general hospitals or those for mental disease. The lesion seems to have no constantly associated pathologic change.

The question was: What effect would a space-consuming mass have on the mental processes of the possessor? On the basis of the cases reviewed, there is no single factor with which one can associate it. The effect on the sensory nerves in the dura of a slow local "pull" of the dura attached to the enostoses must differ from that of the general "push" of the dura due to swelling of the brain (felt in certain acute or chronic experiences). Patients with enostoses rarely are recorded as complaining of subjective symptoms, such as fulness, headache or a feeling of heaviness or pressure in the head. If roentgenograms of the skulls of patients were made on admission to the hospital and at yearly intervals, metabolic determinations and postmortem examinations also being carried out, one would have data on the presence of bony changes in the skull. One would also know whether the growth was progressive and productive of symptoms. This program can be carried out only where the population is stable, laboratory facilities are available and there is an active autopsy service.

In the pathologist's examination of the body, more attention could well be focused on the skull. A hand lens can be utilized to view the inner table. Photography can be employed and comparative histologic studies of the dura in different loci carried out. Besides these observations, the involved bone should be examined chemically and histologically. The present doubt of the character of the nodular lesion—whether due to inflammation, new growth, sluggish circulation, metabolic influence or arteriosclerosis—would then be clarified.

SUMMARY

1. A review of 3,250 protocols from hospitals for mental disease shows calvarial enostoses in 230 patients, or 7 per cent.

2. Of these 230 patients 181 were women and 49 men.

3. The weight of the liver was lowered in 105 cases, the average being 815 Gm.

4. One hundred patients were under 5 feet and 6 inches (167.5 cm.) in stature.

5. Seventeen patients were obese, but 53 were emaciated, while the majority were in the "fairly" or the "poorly" nourished group.

6. Seventy-four patients had atrophy of the frontal portion of the brain (a common change in mental disease but not in mental defect), while 156 did not.

7. In 20 cases in which the pituitary was examined histologically no constant change was observed.

8. Plans are presented for a clinical and pathologic attack on this problem.

CONCLUSION

No consistent correlation was made in the 230 cases between enostosis and any other pathologic condition.

A further communication on this subject will appear in this journal.[18]

The members of the department of pathology of the Harvard University Medical School gave helpful suggestions in the preparation of this paper, especially Drs. S. B. Wolbach, G. A. Bennett and Sidney Farber, and Dr. Merrill C. Sosman made and read the roentgenograms.

18. Canavan, M. M.: Enostoses Within the Calvarium: Survey of Skulls in the Warren Museum of the Harvard University Medical School, Arch. Neurol. & Psychiat. **38**:1249 (Dec.) 1937.

NATURE OF THE "SILVER CELLS" OCCURRING IN MULTIPLE SCLEROSIS AND OTHER DISEASES

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DISCOVERY OF "SILVER CELLS"

In 1928 Steiner [1] announced that he had demonstrated spirochetes in the brain of a patient with multiple sclerosis by means of an improved silver impregnation method. He has since described spirochetes in other brains showing typical lesions and free from suspicion of syphilis. In all of seven of twenty-eight cases of multiple sclerosis examination of the brain gave positive results.[2] Some of these structures lay free in the tissues and others within cells. Some were knobbed, looped or stippled. These spirochetes, which were slightly winding and flatter than Spirochaeta pallida, Steiner caller Spirochaeta myelophthora. He explained their rarity in the brain by their extreme lability, which causes their rapid disappearance directly after the onset of the attack.

Far more common than the complete rodlike structures were certain characteristic elements which Steiner named "silver cells" (*Silberzellen*). They consist of spherical bodies, about the size of the nucleus of a lymphocyte, containing black, dustlike particles of precipitated silver or at times a black, slightly curved particle at one pole of the cell, or a single ring, loop or disklike form. Steiner observed these structures to be present in practically all cases of multiple sclerosis and dementia paralytica in which he made examination and to be absent in all of a large number of brains containing lesions of various other types which were used as controls. He advanced the hypothesis that the argentophilic granules represent fragments of phagocytosed spirochetes.

Read before the Boston Society of Psychiatry and Neurology, Oct. 15, 1936.

From the Department of Neurology, the Harvard University Medical School, and the Neurological Unit, the Boston City Hospital.

The fourteenth of a series of studies the expenses of which have been defrayed by the Multiple Sclerosis Fund of the Harvard University Medical School.

1. Steiner, G.: Spirochäten im menschlichen Gehirn bei multipler Sklerose, Nervenarzt **1**:457 (Aug. 15) 1928.

2. Steiner, G.: Krankheitserreger und Gewebsbefund bei multipler Sklerose, Berlin, Julius Springer, 1931, vol. 8.

Steiner's work has been repeated by Rogers,[3] Kopeloff and Blackman [4] and others. These investigators all agreed that the silver stain is beautifully sharp and specific for spirochetes and that the "silver cells" occur in cases of multiple sclerosis, with occasional exceptions, and in cases of dementia paralytica but in none of a considerable number of cases used as controls. No author other than Steiner has been willing to commit himself as to the presence of spirochetes in sections in cases of multiple sclerosis on the basis of Steiner's stain.

OBJECT AND METHODS OF THE PRESENT STUDY

A further repetition of Steiner's work was undertaken, first, to determine more closely the nature of the "silver cells" by the use of other stains on adjacent sections and, second, to extend the series of controls. Recent work has suggested the possibility that the lesions of both multiple sclerosis [5] and dementia paralytica [6] may be due to local stasis in the smaller blood vessels, and it appeared to us of interest to see if thrombotic and hemorrhagic lesions which bear a certain resemblance to these diseases also contain "silver cells." Curiously, few such cases have been included in the control series of other investigators.

In performing the silver stain, Steiner's most recent instructions [2] were painstakingly followed. All sections were rejected which did not fulfil the criteria which he laid down, namely, that spirochetes should be clearly stained in known syphilitic material run through simultaneously and that no more than a trace of diffusely precipitated silver should be observable.

For comparison, adjacent frozen sections from the same block of tissue in the cases of multiple sclerosis were stained by various means—cresyl violet, gallocyanine, sudan III and the Masson and Spielmeyer methods. In addition, some were subjected to micro-incineration (by courtesy of Dr. Leo Alexander).

The material consisted of blocks of tissue in two cases of multiple sclerosis, chosen because they contained numerous fresh lesions, and in eight cases of thrombotic and hemorrhagic diseases of various types. In five of the cases used as controls the disease was apparently of arteriosclerotic origin, and in two, of traumatic; in the eighth case there was "hemorrhagic encephalitis" of obscure nature. The material in five of these cases was secured from the laboratory of the Boston State Hospital, by courtesy of Dr. Leo Alexander. No attempt was made in the control material to carry out comparative stains on sections adjacent to those used for Steiner's stain, but preparations from the vicinity were already available among the general autopsy slides.

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3. Rogers, H.: The Question of Silver Cells as Proof of the Spirochaetal Theory of Disseminated Sclerosis, J. Neurol. & Psychopath. **13**:50, 1932.

4. Kopeloff, N., and Blackman, N.: Silver Cells (Steiner's Method) in Multiple Sclerosis Compared with Their Presence in Other Diseases, Arch. Neurol. & Psychiat. **34**:1297 (Dec.) 1935.

5. Putnam, T. J.: Evidences of Vascular Occlusion in Multiple Sclerosis and "Encephalomyelitis," Arch. Neurol. & Psychiat. **37**:1298 (June) 1937.

6. Merritt, H. H.; Putnam, T. J., and Campbell, A. C. P.: The Pathogenesis of the Cortical Atrophy Observed in Dementia Paralytica, Arch. Neurol. & Psychiat. **37**:75 (Jan.) 1937.

RESULTS

Multiple Sclerosis.—Steiner's stain is one of the most beautiful available for demonstrating spirochetes, and the sections from syphilitic material were exquisite. In both cases of multiple sclerosis "silver cells" were easily seen, and in one they were so plentiful as to constitute the majority of infiltrating elements in the adventitial spaces (fig. 1 *A*). These cells are observed principally in the adventitia of blood vessels situated toward the periphery of the plaque, as if they represented an early stage in its evolution. In the center of the plaque,

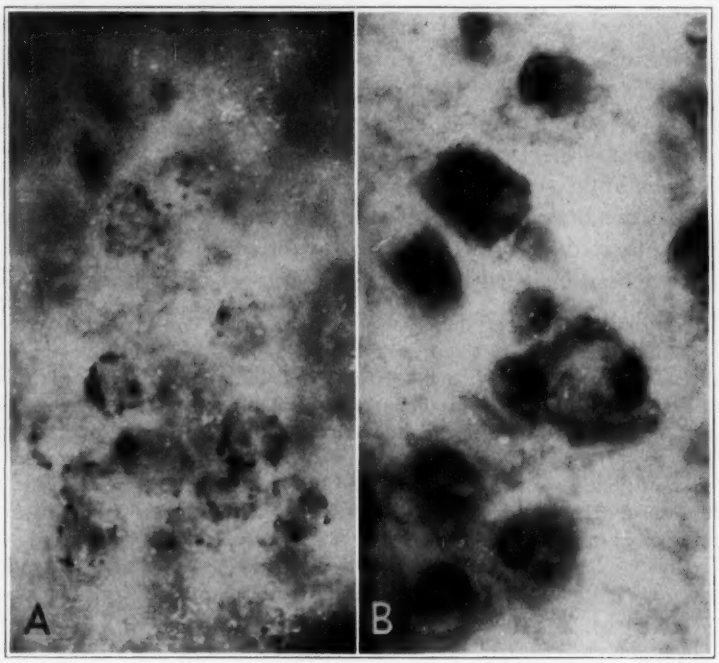

Fig. 1.—Cells lying in the adventitial lining of a vessel in a case of multiple sclerosis. *A*, stained by Steiner's method, shows preponderance of typical "silver cells," and *B*, stained by Masson's method, a continuation of the same vessel in an adjacent section. Oil immersion lens.

where the lesions are older, the "silver cells" are much rarer and in certain lesions are absent. Only in recent, fresh plaques or in older ones which are apparently enlarging does one see the "silver cells" in their most typical aspect.

Homologous areas in adjacent areas stained by other technics showed that the corresponding cells had round or slightly oval nuclei, from about 6 to 8 microns in diameter, with a moderate amount of dispersed chromatin. The cell body was lightly stained with cresyl violet and varied from a small rim to about twice the diameter of the nucleus

(fig. 1 *B*). It contained particles, many of which were yellow or light brown. Sections stained for fat and others stained for myelin showed neither of these substances in the cells, as has already been pointed out by Steiner.[1] The micro-incinerated sections demonstrated gleaming yellow and white particles (fig. 2) which, according to Dr. Alexander, were strongly suggestive of iron and calcium salts.[7]

The general character of the cells appears to indicate that they are phagocytes of glial rather than of hematogenous origin. This agrees with Steiner's belief.

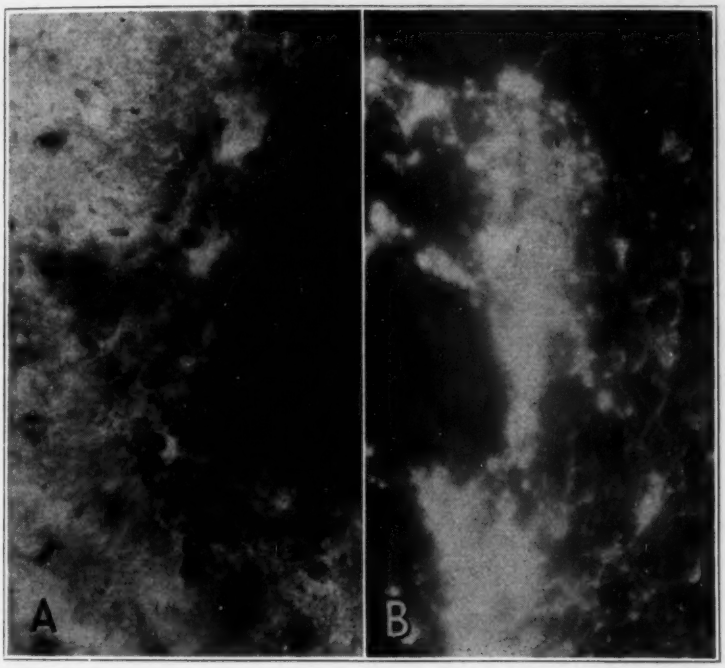

Fig. 2.—Cells lying in the adventitia of a vessel in a case of multiple sclerosis. *A*, stained by Steiner's method, shows preponderance of typical "silver cells," and *B*, subjected to micro-incineration, the same vessel in an adjacent section, and the heavy deposit of iron and calcium salts. High dry lens. Courtesy of Dr. Leo Alexander.

Cases Used as Controls.—In all these cases the red cells and phagocytes containing blood pigment were deeply stained. In three of them typical "silver cells" were seen. As the question may fairly be raised

7. Alexander, L., and Myerson, A.: The Mineral Content of Various Cerebral Lesions as Demonstrated by the Microincineration Method, Am. J. Path. **13**: 405, 1937.

whether syphilis or other infections or multiple sclerosis might be present in these cases, brief protocols are presented.

CASE 1.—N. P., a woman aged 50, with hypertension and arteriosclerosis, complained of headache and loss of memory for a year before death. Ten days before death she became comatose and fell. The clinical picture was consistent with a diagnosis of subdural hematoma of the posterior fossa, and a suboccipital exploration was carried out, revealing a hemorrhage in the cerebellum. She died three days after this, having had a slight rise in temperature the day before. There was no evidence of syphilis, and the Wassermann reaction was negative for both the blood and the spinal fluid.

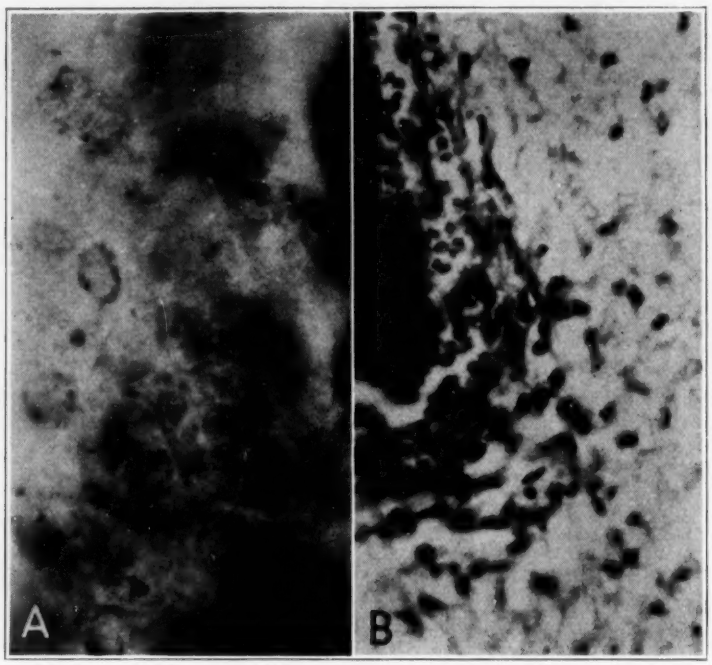

Fig. 3.—*A* (case 1), group of typical "silver cells" lying in the adventitia of a vessel in a case of cerebellar thrombosis (Steiner's stain; oil immersion lens), and *B*, type of infiltration seen in the vicinity of cells shown in *A* (cresyl violet stain; high dry lens).

The lungs showed a mild degree of bronchopneumonia. The blood vessels of the brain were sclerotic. There was a hemorrhagic cyst in the cerebellum.

Microscopic examination of the neighborhood of the hemorrhagic area showed that degeneration was in active progress. The softened area contained a moderate number of large phagocytes and a few clusters of polymorphonuclear leukocytes. In the white matter of the more normal tissue surrounding the cysts, intra-adventitial infiltration was seen about several vessels. The infiltrating cells appeared to be of glial origin, although some might be taken for lymphocytes (fig. 3 *B*). Leukocytes were not observed. Nothing resembling bacteria was seen in typical sections stained with methylene blue (methylthionine chloride).

It was about such vessels in the vicinity of the cyst that "silver cells" were observed in moderate abundance (fig. 3*A*). They were seen as spheres (nuclei?), the surface of which was covered with dustlike granules. At a critical focus they appeared as circles of dots. These circles never lay in apposition with each other but were always separated by a zone, several microns wide, suggesting a rim of protoplasm. In a typical vessel approximately one half of all the cells within the adventitia had such an appearance. The slides were technically excellent and contained no diffuse precipitate.

CASE 2.—A woman aged 54 was known to have had hypertension for two years before death. She had had numerous attacks of coma and occasional convulsions. She was brought to the Boston State Hospital because she became aphasic,

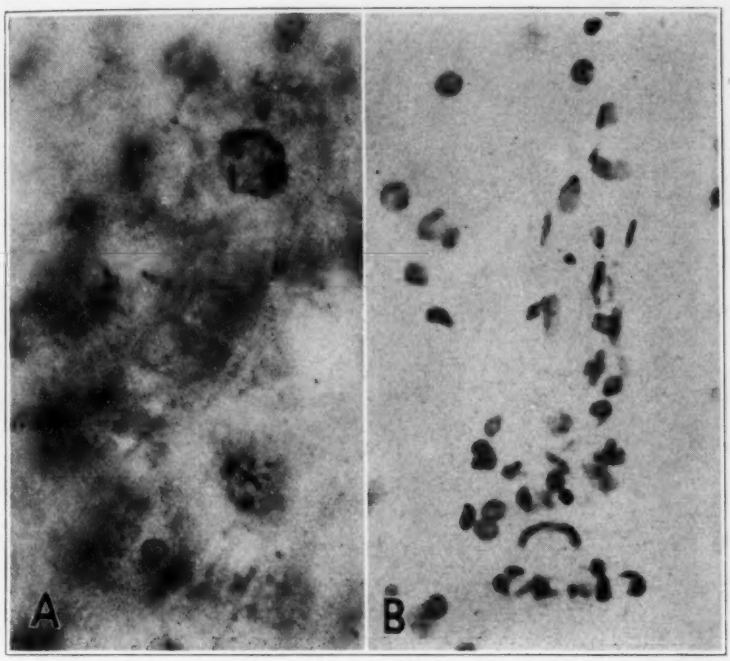

Fig. 4.—*A*, three "silver cells" in a case of cerebral thrombosis (case 2) (Steiner's stain; oil immersion lens); *B*, type of infiltration seen about the vessels in the vicinity (cresyl violet stain; high dry lens).

noisy and difficult to control. Neurologic examination showed no abnormalities. The spinal fluid contain 9 lymphocytes and had a total protein content of 68 mg. per hundred cubic centimeters. The Kahn and Hinton tests of the blood and spinal fluid gave negative results. The patient had a slight fever for ten days, deteriorated gradually and died.

Autopsy (Dr. N. N. Raskin) revealed: three old infarcts of the brain, slight pulmonary congestion, cirrhosis of the liver and cholelithiasis.

Microscopic preparations from the vicinity of an infarct in the temporal lobe revealed the usual evidences of degeneration of cerebral tissue, which in this instance had progressed to the early stages of glial repair. The white matter a

few millimeters from the cavity of the cyst contained many veins surrounded by intense intra-adventitial infiltration. The cells within the adventitial meshes appeared to be of glial origin (fig. 4 *B*). Rarely did one resemble a lymphocyte. Most of them contained little or much yellowish or brownish (hematogenous?) pigment. In sections stained with cresyl violet nothing resembling bacteria was seen.

Blocks for the Steiner stain were also taken from the walls of the cyst. The stain was technically satisfactory, with a minimal amount of precipitate, and spirochetes were stained in syphilitic material run through simultaneously. In the sections from the brain in this case, a small number of typical "silver cells" (fig. 4 *A*) were observed in the adventitia of small veins in the white matter. They

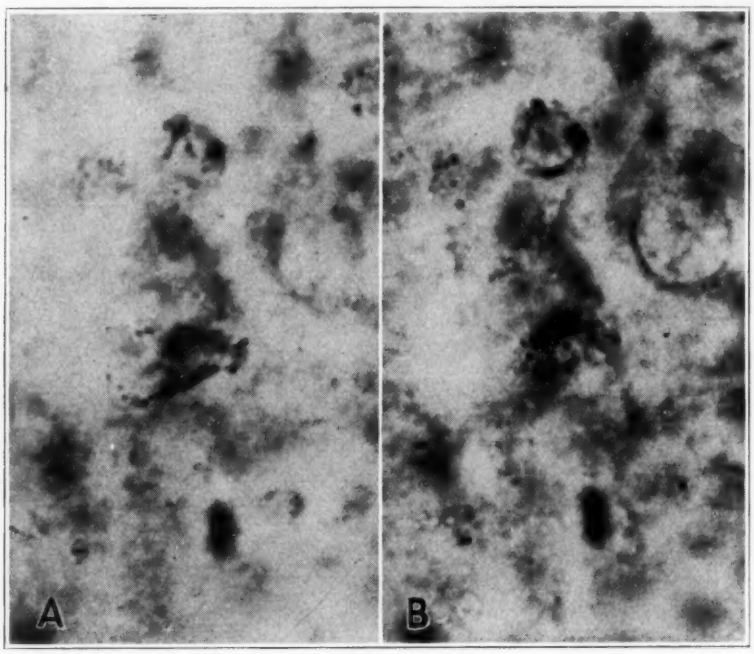

Fig. 5.—*A*, two "silver cells" in a case of cerebral thrombosis (case 3). One contains a spirochete-like structure. *B*, the same section as that shown in *A*, with slightly different focus, illustrates the numerous silver granules in this cell. Steiner stain; oil immersion lens.

occasionally made up approximately one fourth of the nuclei in the wall of the vessel. In addition, larger cells containing coarser aggregates of material which stained with silver were fairly numerous. On the whole, however, the infiltration was considerably slighter than in the sections stained with cresyl violet.

Case 3.—A man aged 68, who was admitted to the hospital without a detailed history, was confused, disoriented and untidy, with hemiplegia and aphasia. The blood pressure was 190 systolic and 110 diastolic. The pressure of the spinal fluid was 250 mm.; the fluid was bloody. The Kahn tests of both the blood and the spinal fluid gave negative results. The patient died after three weeks in the hospital.

Autopsy (Dr. N. N. Raskin) showed: arteriosclerosis, cerebral hemorrhage in the right hemisphere, chronic myocarditis and bronchopneumonia.

The right centrum ovale was occupied by a large blood clot. Sections taken from the edge of the softened area showed early stages of repair and surprisingly few infiltrated vessels. Glia cells, most of which contained fine particles of yellow pigment, were the only infiltrating elements. No bacteria were seen in cresyl violet preparations.

Steiner's stain was satisfactorily carried out on similar sections from the same vicinity. A few unmistakable small "silver cells" (fig. 5) were observed in the adventitia of veins of the white matter. They made up as many as one half of all the infiltrating cells about some vessels.

In one cell a structure resembling a spirochete was observed. It was about 7 microns long and was finely spiral (fig. 5). It represented possibly merely a row of fine granules which the cell contained.

SUMMARY AND CONCLUSIONS

"Silver cells" are characteristic of multiple sclerosis. They appear to be phagocytes of glial origin, as Steiner has described, and often contain yellow pigment.

They are not confined to multiple sclerosis and syphilis, however. They may occur also in vascular lesions under conditions which appear substantially to exclude the possibility of local phagocytosis of micro-organisms. They have not been observed by previous investigators in cases of a great variety of other conditions used as controls.

Small though this material is, it appears sufficient to justify the conclusion that the argentophilic particles are not necessarily of spirochetal or bacterial origin. Their occurrence in vascular lesions, the fact that similar cells contain yellow pigment and the demonstration in them of what is presumably iron by means of micro-incineration suggest that the silver-staining material may be of hematogenous origin.

CLINICAL EVALUATION OF USE OF FLUIDS IN TREATMENT OF DELIRIUM TREMENS

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Until about three years ago patients with delirium tremens admitted to the psychiatric department of the Cincinnati General Hospital were treated under a regimen which included definite limitation of fluids. That the hydration capacity of brains of patients with delirium tremens is above the average was indicated by the observations of Nuzum and Le Count.[1] My associates and I had decided on the restricting of fluids, presumptively with the notion that limiting the available fluids in the body generally should help to combat the cerebral edema that is universally present in delirium tremens. Our treatment, including the low fluid ration, consistently yielded a low death rate and resulted in a comparatively short average stay in the hospital for patients who recovered.

Despite these favorable results, however, there arose a question regarding the rationale of limiting fluids in this state. Since the condition is one in which more or less general intoxication exists, urinary elimination needs to be encouraged and active circulation is necessary, were we not interfering with our own purposes by adding to the intoxication with intensive dehydration and by limiting the urinary output and depressing the circulation? Were we naive in supposing that mere reduction in the fluid intake would have a direct action on the existing cerebral edema? In an attempt to find the answer to these questions, the following empirical experiment was conducted.

Three hundred consecutive cases of delirium tremens, during a period of two and a half years, were arranged alternately so as to form two chronologically parallel series, each including 150 cases. The only requirement for inclusion in this group was the diagnosis of delirium tremens. The patients were assigned alternately according to the order of admission to the hospital, regardless of age, sex, color or coincident disease other than delirium tremens. In a review of the accumulated data concerning these patients, it was found that the two series were sufficiently similar to permit a comparison of the end-results. The age

1. Nuzum, F., and Le Count, E. R.: The Ability of Brain Tissue to Take up Water in Delirium Tremens and Other Conditions, J. A. M. A. **67**:1822 (Dec. 16) 1916.

curve for one series showed no significant fluctuation from that for the other. One series included 146 men and 4 women, and the other, 144 men and 6 women. One series was made up of 125 white persons and 25 Negroes, while the other included 129 white persons and 21 Negroes. Of the patients who recovered, each series included the same number with complicating disorders. It is true that in general the complications were somewhat more serious in the series in which fluids were forced. It is difficult, however, to decide how to weigh this factor, since in a large majority of the entire group of 300 patients recoverability from the delirium tremens did not seem to be affected significantly by the presence of complicating disease.

The items of the treatment given in the two series were the same, except the quantities of fluids administered. The details of the treatment were as follows:

1. No alcohol was given the patient from the time he came under our direction.
2. Absolute rest in bed was ordered.
3. Close observation on the part of the ward personnel was insisted on, in order to minimize the patient's chances of injuring himself or others.
4. Extract of cascara sagrada, 10 grains (0.6 Gm.), was given on admission, followed by 1 ounce (31 Gm.) of magnesium sulfate by mouth two hours later.
5. Magnesium sulfate, 1 ounce (31 Gm.), was given orally every morning for three days, unless there had been more than four bowel movements on the previous day.
6. Alkalis in the form of imperial drink were given three times a day.
7. Drainage of the spinal fluid was carried out as soon after the patient's admission as possible and was repeated as often as was indicated by the course of the illness.
8. Fifty cubic centimeters of a 50 per cent solution of dextrose was given intravenously four times a day.
9. Ten cubic centimeters of a 50 per cent solution of magnesium sulfate was given intramuscularly two times a day for two days.
10. Caffeine with sodium benzoate, 7½ grains (0.48 Gm.), was given hypodermically every four hours for six doses.
11. The patient was digitalized in from thirty-six to forty-eight hours and was then placed on a maintenance dose of the drug.
12. Paraldehyde (100 per cent), 3 or 4 drachms (11.5 or 15.5 Gm.), was given from one to three times a day for sedation.
13. A high caloric, soft or liquid diet was given, supplemented by vitamin-containing substances, especially of the B group. If the patient had difficulty in retaining nourishment, gastric lavage with a solution of sodium bicarbonate was carried out.
14. Fluids were given according to the terms of the experiment.
15. If the patient was asleep, he was not awakened for any reason, medicinal or otherwise.

The sole predetermined difference, then, in the management of the two series of patients consisted in the quantities of fluids given to each.

In one group the fluid intake per patient was limited to 1,000 cc. or less per twenty-four hours; in the other fluids were forced to between 3,000 and 4,000 cc. per patient per twenty-four hours. If patients in the group in which fluids were forced did not cooperate, fluids were given by hypodermoclysis. It is to be regretted that, because of the general absence of cooperation in these patients and the lack of sufficient hospital personnel, it was not possible to measure the urinary output of the patients.

The one detail of the treatment in both series which was permitted to vary according to the course of the illness was the number of drainages of spinal fluid performed in each case. Except in 1 case, in which lumbar puncture was attempted without success, all the readily available spinal fluid was drained shortly after admission to the hospital. Thereafter, repeated drainages were performed only when the patient showed no response to treatment within forty-eight hours. With the lack of response to treatment as a guide, the number of drainages of spinal fluid performed in the two series was as follows:

	Series in Which Fluids Were Limited	Series in Which Fluids Were Forced
No. patients receiving one drainage of spinal fluid	126	94
No. patients receiving two drainages	14	37
No. patients receiving three drainages	1	5
No. patients receiving four drainages	1	3
No. patients receiving five drainages	0	1
No. patients receiving six drainages	0	1
Total no. patients receiving more than one drainage of fluid	16	47

When this table is interpreted in general and it is recalled that the reason for making more than one drainage of spinal fluid in any instance was inadequate response to treatment, it is found that in a large majority of cases in both series the course of the delirium tremens was sufficiently satisfactory that only one lumbar puncture was made. The table indicates, however, that the illness ran a stormy course in appreciably more cases in the series in which fluids were forced than in that in which they were limited.

SUMMARY AND COMMENT

There were 8 deaths in each series—a crude death rate of 5.3 per cent. Of the patients with a forced intake of fluids who died, 5 presented complications which were of sufficient severity to have been possible causes of death without the coincident delirium tremens. Four of the 8 patients receiving limited fluids who died showed complica-

tions of similar seriousness. The number of deaths, then, give little on which to base a decision as to whether it is better to force or to limit fluids in treatment of delirium tremens.

The criteria for discharge from the hospital were the same in both series. The average stay in the hospital of the 142 patients who had been under a regimen of forced fluids and had recovered was four and seventy-five hundredths days, and that of the same number of patients who had limited fluids was four and sixty-five hundredths days. The absence of a significant difference is obvious (table).

It has been demonstrated, then, that in two series which were sufficiently similar and in which the patients were subjected to the regimen that has been described the clinical end-results apparently did not vary with the different amounts of fluid given. A comparative examination of the course of the disease in the two series, based on the number of lumbar punctures done in each series, showed that in a large majority

Analysis of Data on Stay in Hospital

	M	σ	σM	$\sigma M_1 - M_2$
Series in which fluids were forced	4.75	2.74	0.23	
Series in which fluids were limited	4.65	2.24	0.19	
d	0.10	....	....	0.36

In the table, σ indicates the standard deviation of the distributions; σM, the standard error of the means; $\sigma M_1 - M_2$, the standard error of the difference between the means of the two series; (this figure must be 3 or larger, in order that the difference found may be regarded as reliable), and d, the difference between the means of the two series.

of cases the delirium tremens ran a satisfactory course regardless of whether fluids were limited or forced to the designated quantities. Examination of this factor, however, also indicated that there was a greater incidence of cases in which the course was stormy with the regimen of forced fluids than with that of limited fluids. The conclusion seems to be indicated that in most cases of delirium tremens in which the prescribed treatment is administered the quantity of fluid given the patient (up to 4,000 cc. daily) has no significant effect on the course of the illness but that in an appreciable minority of cases the giving of greater quantities of fluids is likely to coincide with the display of more severe symptoms.

In performing drainage of spinal fluid on these patients, as much fluid was removed from each patient as was readily available; that is, lumbar puncture was done with the patient lying on his side, and the fluid was allowed to escape until the drops were far apart. The initial drainage, performed on all patients shortly after admission and before a prescribed regimen of fluids had been established, yielded an average quantity of spinal fluid per patient which was practically the same in both series and which, for the patients receiving only one lumbar punc-

ture, averaged 31 cc. On examining the quantities obtained from patients who were subjected to more than one drainage, however, and who, therefore, had been on either the regimen of forced or that of limited fluids for an appreciable period before the subsequent lumbar punctures, a marked difference was noted. In the 16 cases in the series in which fluids were limited, an average drainage of 22 cc. of spinal fluid was yielded for each lumbar puncture after the first, or 29 per cent less than the average amount obtained at the time of admission. In the 47 cases in the series in which fluids were forced, an average drainage of 37 cc. of spinal fluid was yielded for each lumbar puncture after the first, or 19 per cent more than the average amount obtained at the first puncture. The discrepancy here is so marked that it is difficult to refrain from drawing the conclusion that the greater the quantity of fluid given the more free fluid there is likely to be in the central nervous system. If this is true and if the hydration capacity of the brain in delirium tremens is increased above the normal, one might justifiably postulate that forcing fluids in delirium tremens increases the available free fluid in the central nervous system and consequently causes an increase in cerebral edema in this condition.

That repeated drainages were not performed, however, in all our cases, that the number in which they were carried out was not large and that several details of our treatment have a measurable effect on the water balance in the body generally make these findings difficult of specific interpretation. They are not conclusive enough to permit arbitrary decision favoring strict limitation of fluids in treatment of delirium tremens, particularly since, even if one were able to prove definitely that an increase in fluids in delirium tremens increases the cerebral edema, one must still remember that other organs and functions of the body can hardly be neglected, or even insulted, in order to alleviate the malfunction of a single tissue.

My deductions from this experiment have been in general as follows: The forcing of fluids in delirium tremens is likely to cause an increase in cerebral edema. Fluids, however, are of value in delirium tremens on two accounts: First, they increase the circulatory efficiency, stimulate renal function and combat toxicity generally, and, second, the patient with delirium tremens is likely to be more comfortable and less restless if he is permitted to have fluids according to his desires. Consequently, it is well in these cases to compromise, first by giving the patient as much fluid as he wants, without forcing it on him, and, second, by administering such medication as dextrose intravenously, magnesium sulfate intramuscularly and caffeine hypodermically, in order to stimulate excretion of fluids and flushing of the tissues generally. This sort of regimen is likely to promote maximal detoxification and may be supplemented by repeated drainages of spinal fluid, when more

direct removal of fluid from the central nervous system is thought to be indicated. In the exceptional cases in which the patient takes extremely little fluid and has a coincident inordinate rise in temperature, fluids should be given by hypodermoclysis, as in toxic conditions other than delirium tremens.

Our adherence to this informal method of administering fluids to our patients has not been marked by any appreciable change in either the death rate or the length of stay in the hospital.

CONCLUSIONS

1. Two parallel series of patients with delirium tremens, each including 150, were given treatment that was similar except that one series received less than 1,000 cc. of fluid daily per patient, and the other, from 3,000 to 4,000 cc.

2. The number of deaths in each series was the same.

3. The average duration of the disease in the patients who recovered showed no significant difference in the two series.

4. Though in the majority of cases in both series the illness ran a satisfactory course regardless of whether fluids were limited or forced, a significantly larger number of the cases in which the symptoms were most severe was found in the series in which fluids were forced.

5. Findings are noted which suggest that limiting the fluid intake diminishes and that forcing fluids increases the available free fluid in the central nervous system of patients with delirium tremens.

6. It is recommended that fluids be neither limited nor forced in delirium tremens, that the patient be given as much fluid as he desires for comfort and that the control of the general body fluids and cerebral edema be accomplished by the judicious use of dehydrants, the maintenance of adequate renal and circulatory function and the drainage of spinal fluid as often as is indicated by the course of the disease.

INTELLECTUAL DETERIORATION IN THE PSYCHOSES

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In the present communication we shall report the results of the first of a series of clinicopsychologic investigations into the problem of intellectual deterioration in the psychoses. The designation "clinicopsychologic" is used purposely, implying a combination not only of resources but of practical needs. By this is meant that in attempting a study of the causes, nature and effects of deterioration one should, we thought, in addition to utilizing the means available for such investigations to both the clinical psychiatrist and the psychologist, be guided by the specific interests and goals of both. An adequate starting-point in a combined approach of this type is afforded by the work that has already been done on the subject, the most important features of which can be presented as follows:

To the clinical psychiatrist the problem of deterioration has always been of great, although predominantly practical, interest. Ever since psychiatrists have attempted to bring order into the chaos of conflicting psychiatric syndromes, it has been noted that in a number of diseases, in addition to the temporary impairment of intellectual function during the acute process, there frequently results a permanent defect which interferes with the adjustment of the patient after the active phase has subsided. The importance of such defect in influencing the future adjustment of the patient is of course evident, and therefore it was appreciated from the beginning that it was of primary importance to have in diagnosis, prognosis, management and treatment of such conditions more adequate means of recognizing this factor and of evaluating its probable effects in the future. In most cases the studies of deterioration in clinical psychiatry have been empirical, and few statistically and scientifically systematized investigations have been carried out. Nevertheless, a great deal of attention has been given to it, as is evidenced, for instance, by the fact that the factor of "dementia" has played an

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important rôle in differential diagnosis, prognosis and institution of treatment.

The psychologist has found his main interest in this phenomenon in its relationship to intelligence in general and to special functions in particular. An important impetus in psychologic investigations of deterioration was afforded by the introduction of intelligence tests; a large number of studies along this line have since been reported, and a great deal has been added to knowledge of certain phases of the problem. It must be emphasized, however, that most of these studies have been of predominantly quantitative, rather than qualitative, nature. Most of the psychologic studies hitherto reported can be classified into three main groups: (1) those employing tests of general intelligence, primarily for the purpose of determining the differences in mental age levels; (2) those making use of separate tests for the purpose of discovering defects in special functions, and (3) those attempting the construction of specific measuring instruments that will be particularly useful in ascertaining intellectual deterioration.

The investigators belonging to the first group have concerned themselves for the most part with quantitative studies and have paid particular attention to the phenomenon of "scatter." In the main, the results of these investigations have shown that, whereas in normal persons and in the mentally deficient the age levels at which failures and passes are intermixed are grouped fairly closely around the mental age level, certain psychotic persons in whom deterioration has occurred tend to show a spread of failures and passes to a number of age levels above and below the mental age level. In other words, they show more scatter than the others (Pressey,[1] Pressey and Cole,[2] Curtis,[3] Wells and Kelley [4] and Beumer [5]). This observation led to an attempt on the part of a number of these workers to investigate the amount or kind of scatter that should be considered abnormal and the possibility of establishing on this basis diagnostic or prognostic criteria (Mateer,[6]

1. Pressey, S. L.: Distinctive Features in Psychological Test Measurements Made in Dementia Praecox and Chronic Alcoholic Patients, J. Abnorm. Psychol. **12**:130-139, 1917.

2. Pressey, S. L., and Cole, L. W.: Irregularity in a Psychological Examination as a Measure of Mental Deterioration, J. Abnorm. Psychol. **13**:285-294, 1918.

3. Curtis, J. N.: Point Scale Examination on the High-Grade Feeble-Minded and Insane, J. Abnorm. Psychol. **13**:77-118, 1918-1919.

4. Wells, F. L., and Kelley, C. M.: Intelligence and Psychoses, Am. J. Insan. **77**:17-45, 1920.

5. Beumer, O.: Scattering in Intelligence Test Scores of Mentally Abnormal Persons, unpublished thesis, State University of Iowa.

6. Mateer, F.: The Unstable Child, New York, D. Appleton and Company, 1924.

Wells [7] and Wallin [8]). It is interesting to note that so far no valid criteria for deterioration in terms of scatter have been established.

The second group of workers has attempted to make use of separate tests for the purpose of devising a method that would furnish insight into the nature of the specific functional disturbances in deterioration. On the one hand is the work of Hart and Spearman,[9] who found that deterioration for the most part is diffuse and involves lowering of the intellectual level as a whole. On the other hand, some studies have indicated that impairment of specific functions may occur in the process of deterioration in certain types of psychoses (Hunt [10]). However, most of this work has been done with the organic psychoses, in which the importance of the loss of memory has been fairly well established (Achilles,[11] Liljencrantz,[12] Wells and Martin,[13] Foster [14] and Landis and Rechetnick [15]).

To the third group belong the work of Babcock [16] and that of Simmins,[17] both of which were attempts to devise special measures for deterioration, using as the basis the assumption that vocabulary is representative of native endowment before the onset of the deteriorating process. The investigations differed, however, in that the former emphasized speed and the fixation phase of memory as the measure of the present intellectual ability, while the latter used nonverbal tests of visual perception, which are free from the disturbing influence of associations of past experiences aroused by verbal and pictorial tests. Both studies yielded positive correlations between the degree of deteriora-

7. Wells, F. L.: Mental Tests in Clinical Practice, New York, World Book Company, 1927.

8. Wallin, J. E. W.: Intelligence Irregularity as Measured by Scattering in the Binet Scale, J. Educ. Psychol. **13**:140-151, 1922.

9. Hart, B., and Spearman, C.: Mental Tests of Dementia, J. Abnorm. Psychol. **9**:217-264, 1914.

10. Hunt, J. M.: Psychological Loss in Paresis and Schizophrenia, Psychol. Bull. **31**:713, 1934.

11. Achilles, E. M.: Experimental Studies in Recall and Recognition, Arch. Psychol., 1920, no. 44.

12. Liljencrantz, J.: Memory Defects in Organic Psychosis, Psychological Monographs, no. 143, Princeton, N. J., Psychological Review Company, 1923, vol. 32.

13. Wells, F. L., and Martin, H. A.: A Method of Memory Examination Suitable for Psychiatric Cases, Am. J. Psychiat. **3**:245-257, 1923.

14. Foster, J. C.: Significant Responses in Certain Mental Tests, J. Applied Psychol. **4**:142-154, 1920.

15. Landis, C., and Rechetnick, J.: Changes in Psychological Functions in Paresis, Psychiatric Quart. **8**:693-698, 1934.

16. Babcock, H.: (*a*) An Experiment in the Measurement of Mental Deterioration, Arch. Psychol., 1930, no. 117, pp. 5-68; (*b*) Dementia Praecox, Lancaster, Pa., Science Press, 1933.

17. Simmins, C.: The Measurement of Mental Deterioration, Brit. J. M. Psychol. **14**:113-120, 1934.

tion and the seriousness of the condition as estimated by physicians and are worthy of note as pioneer attempts in this direction. It is important, however, to mention that the value of these devices in measuring deterioration depends on the validity of the vocabulary score as a measure of native intelligence before the occurrence of deterioration, and this, particularly in the organic psychoses, has by no means been established.

The studies made hitherto have undoubtedly contributed a great deal of knowledge which can be used as a starting-point and an indicator of leads that should be followed in the attempt to gain further insight into the various aspects of the problem. A number of such aspects present themselves for further investigation. The clinical psychiatrist, for instance, is interested in knowing what relationship exists between the premorbid abilities of the patient to adjust himself to the task of living in his particular setting and his present inability to do so. Can one determine just what was injured by the mental disease process and what was the extent of such an injury? Further, can one find any relationship between the fundamental disturbances and nature of the disease process and the defect which has occurred? Finally, is there any relationship between the deterioration in personality components other than intelligence and that in intelligence itself (if such can be clearly defined)? From a psychologic point of view one would, furthermore, be interested in the discovery of a function, or functions, that may be related to special testing devices, whether those that already exist or others that would have to be constructed. Above all, is it possible to speak of various special functions in relation to deterioration, or is it true that the involvement is diffuse and does not show any specific characteristics?

Certain general facts which have come to the fore on the basis of previous studies can be taken as the starting-point of the present work. Clinically, it has been ascertained that different types of deteriorating psychoses show certain specific features. Thus one finds that in some memory and judgment are predominantly involved and in others the affective interests in the environment are especially disturbed. In the case of intelligence tests it has been noted that the scatter which involves passes or failures in tests below and above the mental age is not altogether indiscriminately distributed but shows a tendency toward a relationship between special forms of deterioration and the types of scatter. This relationship, however, is not absolute. Thus, given a number of deteriorated patients all suffering from the same form of mental disease, one usually finds that certain tests are involved in the scatter with significant regularity, but not in all cases. The question comes up, therefore, especially in relation to diagnosis, whether, instead of some one special test that will be uniformly affected in a given condition, it is not more likely that a number of such tests may be utilized

in establishing a specific pattern which will occur as a whole in such diseases, even though any single test may or may not be significant.

PROCEDURE [18]

Three hundred persons were used as the basis of the present study. Two hundred of these were psychotic, and 100 persons of subnormal intelligence were used for the purpose of comparison. Of the 200 psychotic patients, there were 100 with schizophrenia (39 with the hebephrenic, 17 with the simple, 12 with the catatonic, 15 with the paranoid and 17 with an undetermined type). The other 100 patients were suffering from organic psychoses (44 from psychoses due to different forms of syphilis of the central nervous system, 17 from alcoholism and 31 from senile and 8 from miscellaneous organic mental diseases). Since the purpose of this study was to determine whether there are any specific characteristics in the test performance of deteriorated psychotic patients and whether these can be differentiated from the performance of originally mentally defective persons, the material had to be selected in a manner which would permit comparisons. Only persons were used whose intelligence rating fell between the mental age levels of 8 and 12 years. In the case of the mentally defective, we limited ourselves to patients who had a definite history of initial retardation (to exclude the possibility of deterioration). In both groups of the psychoses, we used only patients who had a clear clinical history of an originally, at least, average intelligence and social adjustment (to exclude the possibility of a psychosis engrafted on an original mental defect). No attempt at selection was made with reference to social, racial, cultural or other ecologic factors.

The intelligence tests used were those comprised in the short form of the Stanford-Binet scale. This scale was selected as the instrument of measurement, first, because of the meaningfulness it has obtained through use and, second, because it provides a composite quantitative index made up of a wide sampling of qualitatively different mental activities. Although the use of the short as compared with the complete form presents some disadvantages, it has nevertheless been shown to correlate with the latter to a high degree and can do little more than minimize the findings. Further, the fact that the use of the short form is more general in most clinics would make the results of more specifically practical value.

In order to control the effects of maturation, on the one hand, and senility, on the other, chronological age limits were set at 16 and 45 years, except in the organic disease group, in which, since senility itself may condition the mental disease, the upper limit was disregarded. The range of mental ages in all three groups was, as already stated, from 8 to 12 years. Mental age was also controlled by equating the means and standard deviations for the group in this respect. These, expressed in terms of months, are as follows:

	Means (Months)	Standard Deviation
I. Organic disease group.....	126.3	± 13.8
II. Schizophrenic group.....	126.3	± 14.4
III. Subnormal group.....	126.4	± 11.9

An effort was made to exclude all cases in which performance may have been unduly affected by the presence of language handicap, gross neurologic sensory

18. The superintendent of the Mount Pleasant State Hospital and the director of the Child Welfare Station gave help in procuring some of the case material used in this study.

and motor defects or lack of apparent cooperative effort. All tests were administered by trained examiners under standard conditions in accordance with the prescribed procedures.

RESULTS

Quantitative and Qualitative Analysis.—The groups were first compared with respect to the degree of scatter. Because of the inconsistencies of earlier workers concerning the method of calculating scatter and in order to take into consideration all aspects of irregularity, four measures were employed:

1. Range in terms of test levels (from the level at which all tests are passed to, but not including, that at which all tests are failed).

2. Total number of months failed in range.

3. Sum of the percentages of failure at each test level weighted according to number of test levels from the basal level.

4. Tests passed above and failed below the mental age weighted (1, 2, 3, etc.) according to the number of test levels from that of the mental age.

The groups were next compared with respect to vocabulary level. A divergence score was calculated in terms of vocabulary mental age minus test mental age calculated without vocabulary. In determining the vocabulary mental age level, interpolations were made at the 11, 13, 15 and 17 year levels in accordance with figures given by Babcock.[16a] The test mental age was calculated without vocabulary by reweighting the other tests accordingly. Divergence scores were assigned in terms of months.

The results of these comparisons (table 1)[19] show the average scores of both psychotic groups on all measures to be significantly higher than those of the subnormal group. The average scores of the organic group on all measures are higher than those of the schizophrenic group, although in no case is this difference statistically significant.

Intercorrelations for the scores on the various measures show that in general the measures of scatter are similarly positively related in all three groups, thus supporting the assumption that the measures are all pertinent to some one general factor of variability. The vocabulary measure is positively related to all measures of scatter in the two psychotic groups but not in the subnormal group, suggesting that some systematic factor may operate in the case of the psychotic patients which is absent in that of the subnormal subjects.

19. The complete statistical data for these and subsequent findings are not included here for lack of space. They are reported fully in the thesis of one of us (E. M. P.) available at the library of the State University of Iowa.

In order to determine the more qualitative differences in performance among the groups, a comparison was made of the percentage of each group which passed each single test. For both the schizophrenic patients and those with organic disease as compared with the subnormal subjects certain tests showed a significantly higher percentage of passes, and others, a significantly higher percentage of failures. Tests relatively easy for the patients with organic disease as compared with the subnormal subjects include the vocabulary tests (X_1 XII_1 and XIV_1) and the president and king test (XIV_3). Tests relatively difficult for the patients with organic disease as compared with the subnormal subjects are: counting backward (VII_2), naming digits backward (IX_4 and XII_6) and the date (IX_1), weights (IX_2), three words (IX_5), absurdities (X_2) and associations (X_6) tests. Tests relatively easy for the schizophrenic as compared with the subnormal subjects include: vocabu-

TABLE 1.—*Average Scores for Each Group With Probable Errors and Vocabulary Mental Age Divergence Measures*

Measures	Averages and Probable Errors		
	Organic	Schizophrenic	Subnormal
1. Range in test levels	4.83 (0.0787)	4.66 (0.0800)	3.36 (0.0755)
2. Number of months failed in range	35.64 (0.078)	34.60 (1.187)	23.06 (0.916)
3. Sum of ratio of failure at each test level weighted according to distance from basal level	44.40 (1.575)	42.52 (2.071)	19.77 (0.964)
4. Tests passed above and failed below mental age weighted according to distance from mental age	31.91 (1.191)	30.28 (1.296)	16.88 (0.735)
5. Vocabulary mental age — test mental age without vocabulary	42.42 (1.367)	38.44 (1.507)	0.84 (0.141)

lary (X_1, XII_1 and XIV_1), president and king (XIV_3) and arithmetical reasoning (XIV_5) tests. Tests relatively more difficult for the schizophrenic than for the subnormal subjects include: comprehension ($VIII_3$ and X_5), date (IX_1), weights (IX_2), three words (IX_5), absurdities (X_2), associations (X_6), pictures (XII_7) and problems of fact (XIV_4) tests (table 2).

Thus, two sets of qualitative features differentiate the performance of deteriorated psychotic patients from that of subnormal persons—one characteristic of the performance of the organic group and the other of the performance of the schizophrenic patients. Such qualitative differences go beyond purely quantitative differences in the degree of scatter in that they permit the description of a particular performance both quantitatively and qualitatively in terms of the patterns of scatter, thus presenting a more detailed and meaningful picture of mental function in deterioration. Such patterns of scatter may be thought of as particular configurations of successes and failures dependent on

differences in the difficulty value of the various tests for deteriorated psychotic patients and that for subnormal subjects. As in medicine, diagnosis is determined by the presence not of one symptom but of a complex of symptoms or a special syndrome; likewise, success or failure in one of the differential tests means little. However, a number of such successes and failures (or the presence of a particular pattern of scatter) may be considered to be highly significant of deterioration.

In order to determine their significance in differentiating between the groups, each performance in each group was scored with reference to these patterns, a credit of 1 being given for each success or failure in the differential tests.

TABLE 2.—*Frequency Percentages of Passes and Probable Errors*

Test	I. Patients with Organic Disease	II. Schizophrenic Patients	III. Subnormal Subjects
$VIII_2$	88 (2.21)	95 (1.46)	99 (0.671)
$VIII_3$	97 (1.15)	85 (2.41)	98 (0.944)
$VIII_4$	100 (0)	93 (1.72)	98 (0.944)
$VIII_6$	100 (0)	100 (0)	99 (0.671)
IX_1	58 (3.33)	50 (3.37)	94 (1.66)
IX_2	48 (3.42)	40 (3.89)	77 (2.9)
IX_4	58 (3.37)	70 (2.97)	75 (2.92)
IX_5	69 (3.12)	77 (2.84)	91 (1.93)
X_1	100 (0)	100 (0)	77 (2.9)
X_2	52 (3.37)	33 (3.17)	72 (3.09)
X_3	74 (2.96)	61 (3.29)	85 (2.05)
X_6	26 (2.98)	29 (3.06)	67 (2.65)
XII_1	90 (2.02)	88 (2.19)	36 (3.28)
XII_4	18 (2.63)	33 (3.17)	23 (2.84)
XII_5	27 (3.02)	20 (2.7)	31 (3.12)
XII_6	13 (2.27)	28 (3.03)	27 (2.99)
XII_7	41 (3.35)	37 (3.26)	53 (3.37)
XII_8	36 (3.28)	46 (3.36)	47 (3.67)
XIV_1	58 (3.33)	50 (3.37)	2 (0.944)
XIV_3	18 (2.59)	18 (2.59)	4 (1.32)
XIV_4	24 (2.88)	17 (2.54)	31 (3.12)
XIV_5	13 (2.27)	17 (2.54)	6 (1.6)

The patterns and method of scoring are as follows:

1. Organic pattern

   Credit of 1 for each of the following tests passed in range: X_1 XII_1 XIV_1 and XIV_3.

   Credit of 1 for each of the following tests failed in range: $VIII_2$, IX_2 IX_4, IX_5, X_2, X_3, XII_8 and IX_1.

   The score equals the total number of credits.

2. Schizophrenic pattern

   Credit of 1 for each of the following tests passed in range: X_1, XII_1, XIV_1, XIV_3 and XIV_5.

   Credit of 1 for each of the following tests failed in range: $VIII_2$ IX_1, IX_2, IX_3 X_2, X_3, X_6 XII_7 and XIV_4.

   The score equals the total number of credits.

With respect to both patterns, the two psychotic groups showed significantly higher average scores than the subnormal groups. Although

the patterns differentiate to some extent between the two psychotic groups, the differences here are not statistically significant.

In order to determine the significance of a particular pattern score as indicative of deterioration, a comparison was made of the percentage of each group failing at or above the various score levels (table 3). With respect to the schizophrenic pattern, 72 per cent of the patients with organic disease as compared with 2 per cent of the subnormal subjects obtained scores of 6 or higher. Similarly, 72 per cent of the patients with organic disease as compared with 7 per cent of the subnormal subjects obtained scores of 6 or higher. Thus, when one rules out such factors as lack of cooperation, gross neurologic sensory and motor defects or language handicaps which may interfere with per-

TABLE 3.—*Comparisons of Percentages for Subnormal and Psychotic Subjects Failing at or Above the Various Pattern Score Levels*

	I. Organic Pattern		II. Schizophrenic Pattern	
Score	Subnormal Subjects	Patients with Organic Disease	Subnormal Subjects	Schizophrenic Patients
0	100	100	100	100
1	97	100	98	100
2	84	100	81	100
3	61	100	54	99
4	29	100	31	94
5	17	89	11	84
6	7	72	2	72
7	2	50	1	56
8	0	25	1	35
9	0	14	0	21
10	0	3	0	11
11	0	0	0	9
12	0	0	0	5
13	..	..	0	0
14	..	..	0	0

formance, a score of 6 or higher with reference to these patterns can be considered highly significant of deterioration. The patterns of scatter, then, although they cannot be used as final diagnostic measures, are useful as supplementary diagnostic aids in differentiating psychotic deterioration from congenital defect. Although the patterns are too overlapping to be of any diagnostic value in differentiating the schizophrenic and the organic groups, the fact that each psychotic group obtained a higher average score with respect to its own pattern, plus the fact that a number of the subtests were significantly more difficult for one group than for another, suggests that with a finer scale of measurement a significant differentiation may be revealed.

The significance of the scatter patterns as characteristic of deterioration may be observed further in their relation to the degree of deterioration, duration of disease and differential diagnosis. The estimated original mental age minus the test mental age was taken as the measure of the degree of deterioration. Estimations of original mental

ages were made in accordance with the Binet mental age corresponding to the grade status as determined by Otis. With regard to duration of disease, subjects were rated on a five point scale as follows:

1—less than 6 months
2—6 months to 1½ years
3—1½ years to 3 years
4—3 years to 6 years
5—6 years or more

These divisions were selected because they most nearly approximate the natural divisions presented by the data.

The scatter pattern in both groups shows a low, but definitely positive, relationship with the degree of deterioration, the correlation for both groups being 0.35. Although the vocabulary divergence measure has a correction of 0.47 with the degree of deterioration in the schizophrenic group, this correlation is only 0.29 for the organic group. It must be emphasized here that measures of degree of deterioration can hardly be evaluated until there is available a more reliable measure of undeteriorated intelligence than can be furnished by the school history. The patterns, however, which consider both quantitative and qualitative factors are of value in that they suggest lines of experimental investigation for the determination of more reliable measures.

Concerning duration of disease, the relationship in both groups approximates zero. This is consistent with the fact that in some conditions deterioration is more rapid than in others. Further, the tendency toward a negative relationship in the schizophrenic group is interesting in light of the fact that in those conditions in which deterioration is the most likely it tends to be most rapid.

There is no significant relationship between the pattern scores or the vocabulary divergence scores and differential diagnosis. However, that the senile subjects show a slightly higher average score with respect to both the pattern and the vocabulary measure than either the alcoholic or the syphilitic patient is interesting in light of the fact that senile patients show more diffuse cortical involvement. Similarly, in the schizophrenic group the fact that the hebephrenic type shows a higher average score for both the pattern and the vocabulary measure than any of the other types of schizophrenia is consistent with clinical observations of the rapid and extreme deterioration associated with schizophrenia of the hebephrenic type.

ANALYSIS OF PATTERNS AND INTERPRETATION

More important than the diagnostic value of these scatter patterns is the light which they throw on the qualitative nature of deterioration. An analysis of the tests composing the patterns, with special reference

to differences in both the general and the more specific functional components involved, will make these patterns more meaningful in relation to the deterioration process.

Tests relatively easy for both psychotic groups as compared with the subnormal subjects include the vocabulary tests and the president and king test. That vocabulary for the most part remains relatively unimpaired by the deterioration process has been explained by Babcock [16a] on the basis of its dependence on old learning involving one of the earliest formed response patterns. In a personal communication, Line has suggested an explanation on the basis of the method of testing, which differs from that adopted from the other tests, first, in that the examiner can wait for the response and urge and rephrase the question, and, second, that the test has many units, failure in one or two not being serious—these two factors tending to reduce the effect of variability and thus give a truer picture of native intelligence.

The two explanations appear meaningful in relation to a third factor, namely, the vocabulary test, because of both the nature of its content and the adopted procedure, does not necessitate the directional control of thought required by other tests, wherein the content is dependent on the formation of new associations and the procedure leaves the subject to his own devices once the directions have been given. By directional control of thought is meant the application in the process of thought of certain conative adjustments, mental attitudes and motivational sets which facilitate adaptive thinking. It is apparent that the vocabulary test, which calls for a more or less habitual response, requires less directional control of thought than tests which call for the formation of new associations and which, since there is no habitual response, tend to arouse associations of strong affective value, which must be inhibited in favor of others more pertinent to the desired end. Further, if the subject becomes lost in irrelevant associations, leading him away from the goal, the procedure allows the examiner to reinstate the goal and remotivate the subject with reference to that goal. This explanation applies equally well to the president and king test, which, again, is a test depending on old learning and adoption of a procedure whereby the examiner is permitted to wait for the response and urge the subject until certain of having obtained the best response of which he is capable. This test, it is true, involves the additional function of comparison—a function so basic, however, as not likely to be lost except in the most extreme deterioration.

Tests relatively difficult for both psychotic groups as compared with the subnormal subjects include those of date, weights, three words, absurdities and associations. All these tests, except the date test, which is largely a matter of orientation, differ from those found relatively

easy for the psychotic subjects in that they depend on a rigid directional control of thought. An end must be perceived, new data fixated and new associations formed with reference to that end. The subject not only must perceive a goal but must persist in adaptations toward that goal without the aid of the examiner. In the case of the weights test, for example, the subject may without difficulty comprehend the task and select a suitable method, but to persist in these adaptations toward the goal requires the inhibiting of many irrelevant ideas. The subject may begin to play with the blocks, be curious as to how they are weighted and gradually lose sight of the goal altogether. In other cases, although the goal is not entirely lost, some blocks may be compared carefully, while others are placed without trying them at all. The three word test depends not only on the number and quality of associations but on the readiness with which the particular associations can be called up and combined into a logical whole, the subject at the same time inhibiting irrelevant and incidental associations, which may, however, have far more affective value for him. It is not surprising that subjects whose associations are often based on other than logical connections should find difficulty with such a test. Although detection of absurdities is primarily a test of judgment, it is also one which depends on close attention to the essential elements and hence requires specific conative adjustments. That schizophrenic subjects, in particular, should have difficulty with the associations test is readily understood, since associative disturbance is a primary symptom and their suspicion and evasiveness would bring further interference. Subjects often become trapped within a particular category and, losing sight of the goal, spend considerable time attempting to name words belonging to this particular category. In other instances, the subject may stick to a few words of strong affective value, repeating these words over and over. In still other instances, the subject may be carried away by a particular association and begin to talk in sentences or block altogether.

In all of these tests it is apparent that specific conative adjustments, mental attitudes and motivational sets play an important rôle in determining success and that in this sense they depend on a rigid directional control of thought.

The difficulty of the psychotic subject in giving the date partially corroborates clinical observations of general disorientation in psychoses. Failure in giving the date might be accounted for on the basis either of lack of interest in changes occurring in the outside or of disturbance in memory. The former is probably the more important, although the latter may be a factor in organic disease. Criticism of the use of this test with psychotic subjects has frequently been made on the ground that institutionalized patients can hardly be expected to know the date.

However, the fact that present data show that the same percentage of noninstitutionalized as that of institutionalized patients fail in this test makes such a criticism unwarranted.

Certain tests are relatively more difficult for the schizophrenic than for the subnormal subjects, and others, for the patients with organic disease. Tests relatively difficult for schizophrenic as compared with subnormal subjects include the two comprehension tests and the tests involving pictures and problems of fact. No test can be said to depend on any specific function; rather, all tests are dependent on a number of functions. However, the function of judgment appears to be common to all the tests. That judgment, and particularly ideational judgment involving social purpose, is markedly impaired in the schizophrenic process has long been noted in psychiatric practice. That this defect becomes apparent in the standardized test situation lends experimental support to clinical observation.

The ease of arithmetical reasoning for the schizophrenic subject is more apparent than real, the differential character of the test being chiefly the result of its marked difficulty for the subnormal subjects, who probably have never acquired the operational technic necessary for the solution of the problems.

Tests relatively difficult for the patients with organic disease as compared with the subnormal subjects include both digits-reversed tests and counting backward from 20 to 1. That naming digits in reverse order is not a matter of memory alone is obvious; however, that success in giving digits backward depends first on the ability to retain the digits long enough to reverse the process is equally apparent. The difficulty of this test for the patients with organic disease not only corroborates clinical observations of disturbance in memory frequently associated with organic psychoses but points to additional evidence for the frequent observance in organic psychoses of a tendency to perseveration. The latter observation is further confirmed by failure in counting backward from 20 to 1, a test which, although to some extent a matter of speed, is largely dependent on the ability to shift from a well habituated to a diametrically opposite pattern of response.

The preceding analysis of the tests represented in deterioration patterns shows that certain fundamental functions are involved in the process. It is true that we cannot as yet say that deterioration as a whole is limited to these specific functions. We feel justified, however, in stating that in the psychoses investigated the most prominent feature in the deterioration is disturbance of activities requiring the directional control of thought. More specifically, we can say that in schizophrenia failure occurs most frequently in those tests in which performance is most heavily dependent on practical judgment, whereas in the organic psychoses pathologic perseveration and disturbances in memory are

important features in the deterioration. The value of these results is enhanced by the fact that in clinical observations, too, one finds that these functions are most severely affected.

Further work will, of course, have to be undertaken to establish the justification for such conclusions—the search for a more specific relationship between fundamental function and the disease process and the search for tests which can serve as more adequate criteria for the presence and extent of deterioration.

SUMMARY AND CONCLUSIONS

The present study is an analysis of the performance on the short form of the Stanford-Binet scale of a series of 200 deteriorated psychotic patients and 100 subnormal subjects, in the attempt to find significant differences which may be described in terms of objectively recognizable patterns of scatter differentiating deterioration from congenital defect and giving some insight into its functional nature. The findings may be summarized as follows:

1. The performance of deteriorated psychotic patients differs both quantitatively and qualitatively from that of subnormal subjects at the same mental age level. Not only do psychotic patients tend to scatter more than subnormal persons, but some tests are found to be significantly easier for psychotic than for subnormal subjects and others more difficult.

2. These differences can be described in terms of objectively recognizable patterns of scatter. Such patterns are useful, first, as supplementary diagnostic aids in differentiating deterioration and congenital defect and, second, as means of gaining some insight into the qualitative nature of deterioration.

3. The patterns show a low but definitely positive relationship to the degree of deterioration. No significant relation is found between the patterns and the duration of the disease or the differential diagnosis.

4. On the basis of analysis of the patterns, the hypothesis is advanced that deterioration manifests itself in the material studied in activities requiring the directional control of thought.

5. The study shows the value of psychometry, as furnishing not measurements expressed as a single number or quantity without meaningful relationship to the phenomena being examined but indexes to both quantitative and qualitative changes in underlying psychic function.

MALIGNANT TUMOR WITHIN THE THIRD VENTRICLE

THREE CASES OF UNUSUAL TYPE WITH INVASION OF THE VENTRICULAR WALLS

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AND
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Several months ago, when examining the brain of a patient who had exhibited an unusual and interesting clinical picture, one of us discovered a tumor extending throughout the ventricular system which was quite unlike any of the growths commonly seen in the cerebral ventricles. It was recalled that three similar cases had been observed in this clinic within approximately ten years. On consultation of the records, it was found that the clinical picture in these cases presented many features in common. In two of the older cases the histologic character of the tumor was, indeed, identical with that of the tumor under investigation. In the third case, which would have made a total of four cases, the tissues had been lost, and the descriptions of the sections were scarcely adequate to establish the nature of the tumor. This case has, therefore, been omitted. The three tumors which are the subject of this paper all seemed to arise from the walls of the third ventricle and extended into the lateral and fourth ventricles, destroying the ependyma and infiltrating their walls to some extent. Their histologic characteristics were quite unlike those of the ependymoma or the subependymal glioma. There was a superficial resemblance to the pinealoma, but in each case the pineal body was normal. We have not been able to establish the true nature of these tumors or their exact origin, but we believe that they represent a distinct type of intraventricular tumor, which gives rise to a fairly distinctive clinical picture. We have been unable to find a previous description of such a tumor.

REPORT OF CASES [1]

CASE 1.—*Headache and mild papilledema. Dilatation of the ventricular system Exploration of the posterior fossa, with negative results. Disappearance of symptoms. Polyuria and polydipsia two years later. Unsteadiness of gait and difficulty in speech about four years after the onset. The spinal fluid contained 60*

From the Henry Phipps Psychiatric Clinic and the Neurological Clinic of the Johns Hopkins Hospital and School of Medicine.

1. Dr. Adolf Meyer granted permission to report these cases.

cells per cubic millimeter and a great excess of protein. Progressive dementia and death. Postmortem examination revealed a small growth in the base of the third ventricle and universal, diffuse invasion of the ependyma by neoplastic cells.

History.—W. S., a previously healthy boy aged 15 years, experienced severe headache on April 13, 1932, which lasted for a week and was associated with vomiting. He was taken to a hospital in Baltimore. Examination is said to have shown mild papilledema. The spinal fluid was under a pressure of 210 mm. of water; there were 16 lymphocytes per cubic millimeter; the protein was not increased, and the Wassermann test gave negative results. Medical and neurologic examinations gave otherwise normal results. Roentgenograms of the skull revealed nothing of significance. Ventriculography showed that the lateral and third ventricles were dilated. The third ventricle was perhaps displaced upward a bit, but so slightly that no stress was placed on it. It was thought that the patient had a cerebellar tumor, and the posterior fossa was explored, with negative results. The symptoms rapidly receded, and on May 7 he was discharged, apparently well. On the chance that he might have an undisclosed neoplasm, two courses of high voltage roentgenotherapy were administered in the next few months. The patient returned to school and during the years 1933 and 1934 continued work without difficulty.

No symptoms were observed until August 1934, when, after mild pharyngitis, there suddenly developed excessive thirst, and the boy began to excrete great quantities of urine. It was estimated that he passed 2 gallons (7.5 liters) of urine a day. At the same time he complained of fatigue and began to lose weight. The mother noticed that he was more irritable than previously. There was no complaint of headache and no vomiting.

In October 1935 the patient was reexamined. The polyuria and polydipsia had diminished, but were still present. Neurologic examination gave normal results. Dr. Frank B. Walsh, of the Wilmer Ophthalmological Institute, stated that the optic disks showed no definite abnormality and that the visual fields were of normal outline.

During the last part of December 1935 the patient began to have difficulties in gait and speech. He was readmitted to the hospital on January 7, under the care of Dr. John E. Howard. His behavior was normal, and he was apparently cooperative; however, he could grasp the meaning of only very short, simple sentences, and it was difficult for him to understand what was expected of him in the neurologic examination. He could not always express himself clearly and occasionally employed words in his sentences which were not suitable for his meaning. His vision was normal or nearly normal, but he could not read. There was mild congestion of the optic disks but no real papilledema or atrophy of the optic nerves. The cranial nerves were otherwise normal. The arms and legs were moved freely, and there was no spasticity, weakness or ataxia. The station was unsteady and the gait reeling, but the patient could walk without support. The tendon reflexes were brisk but about equal on the two sides. The plantar reflexes were predominantly of flexor type. Spinal puncture yielded clear fluid under normal pressure; there were 60 lymphocytes per cubic millimeter; the Pandy test gave negative results.

On February 11 the boy had two generalized convulsions, which were followed by mental confusion of several hours' duration. Ventriculography was performed a second time. The ventricular system was somewhat more dilated than at the first examination, but the ventricles were symmetrical. During February 1936 there developed an acute infection of the upper respiratory tract, and the patient's mental condition became worse immediately. He lay on the bed most of the day

with his eyes closed, as if in a stupor. He could be partially aroused but was never quite clear. At times he did not recognize his relatives. There were also periods when he was restless, destructive and emotional. Finally, he refused food and thereafter had to be fed with a tube. There was increasing difficulty in speech and gait. It soon became impossible to care for him properly in a general hospital, and he was transferred to the Phipps Psychiatric Clinic.

Examination.—On March 6, 1936, the patient, aged 19, was poorly nourished and poorly developed. He was apparently aphasic, for he showed no understanding of what was said to him and could not form even simple sentences correctly. His speech was jargon and was frequently incomprehensible. There were also evidences of apraxia, for he was unable to handle familiar objects properly. He would put a pencil in his mouth or try to write with a spoon. He was calm and quiet most of the time, but was sometimes noisy and restless.

On March 17 an examination for aphasia was carried out. The patient frequently seemed to make genuine efforts to cooperate, but he was fatigued easily and became irritated. He was often indifferent and apathetic, and, all in all, his contact was only fair. Some examples of his performance will be mentioned:

1. He counted back from 20 to 1 as follows: 20, 18, 19, 20, 14, 13, 13, 12, 11, 10, 9, 8, 7, 9.

2. He misspelled words like "house" and "animal."

3. He could not say "Methodist Episcopal," although he repeated some test phrases.

4. He pointed to the different parts of his body fairly well. Occasionally he pointed to the wrong side of his body or the wrong limb.

5. He failed to interpret most things he heard.

6. He could not read, pick out words or recognize individual letters or numbers.

7. When given a pencil, he seemed to understand its nature, for he made several ineffectual efforts to write with the wrong end. When the pencil was placed properly in his hand, he could not copy simple geometric designs; he could not write to dictation or copy written or printed words or letters. He did no better with numbers.

8. When given a match-box, he could not get the matches out of the box, although he made several efforts to do so. When a match was placed before him, he picked it up and struck the wrong end clumsily on the table.

9. He could not handle a knife, fork or spoon and could not feed himself.

Neurologic examination gave unsatisfactory results, owing to difficulties in securing cooperation. The gait was reeling, and the patient fell at times if not supported. The tendon reflexes were all active and approximately equal on the two sides, although several observers thought that the right knee jerk was sometimes greater than the left. The plantar reflexes were normal or perhaps equivocal. There was no spasticity or muscular rigidity. Coordination in the finger to nose and heel to knee tests was not definitely altered. The optic disks were thought by some to be mildly edematous, but these changes were never outspoken. Several spinal punctures were performed. The pressure was always elevated, ranging from 220 to 250 mm. of water. There were from 60 to 70 cells per cubic millimeter, which were regarded as lymphocytes. The protein was constantly increased, ranging from 400 to 500 mg. per hundred cubic centimeters. The blood sugar level was normal. The temperature ranged from 96 F. (rectal) to normal.

Course.—The patient was soon confined to bed. On May 9 he became unconscious; breathing was stertorous; general muscular rigidity and twitchings devel-

oped; the temperature rose to 105 F., and the patient died just four years and one month after the onset of the illness.

Autopsy.—Postmortem examination revealed no significant pathologic changes in the body outside the nervous system. The brain was normal externally, except for slight flattening of the convolutions, which was taken to indicate a mild increase in intracranial pressure. The meninges were delicate and transparent. The ventricular system was moderately and universally distended. The dilated ventricles were lined with a soft, spongy, grayish tissue, which had replaced the

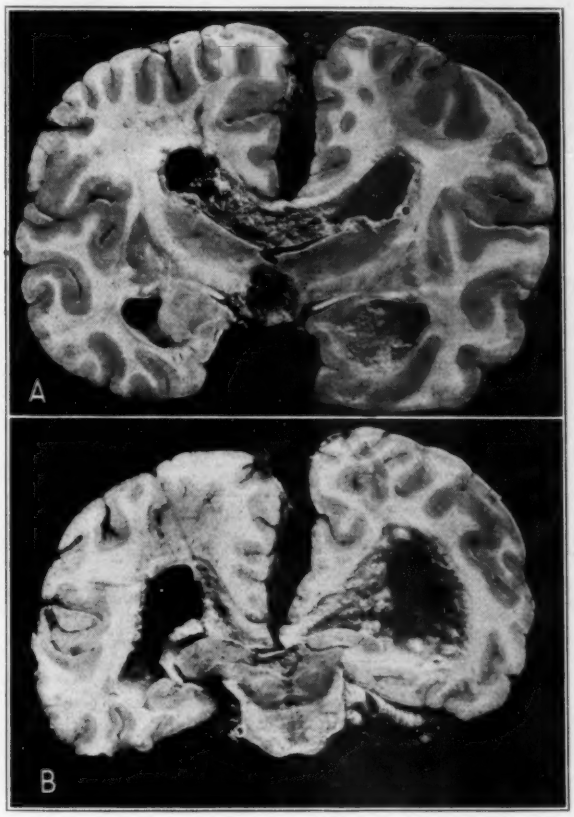

Fig. 1 (case 1).—*A,* section through the cerebral hemispheres, showing distribution of the tumor in the third and lateral ventricles. The fornix and the septum pellucidum have been destroyed, and the lower half of the corpus callosum is infiltrated. The floor of the third ventricle is also invaded. *B,* section through the anterior part of the pons, showing distention of the lateral ventricles and invasion of their walls by tumor tissue.

ependyma almost completely. This tissue, which was composed of tumor cells, extended throughout the third, fourth and lateral ventricles and was seen to some extent in the dilated aqueduct. The thickness of the tumor tissue varied from a few millimeters to almost a centimeter. In the anterior part of the third ventricle was a firm, round, brownish-red tumor nodule, about 1 cm. in diameter.

This tumor infiltrated the floor and walls of the ventricle, destroying part of the infundibulum (fig. 1 *A* and *B*). The soft tumor tissue which extended through the ventricles was in direct continuity with this nodule, which evidently represented the origin of the growth. The walls of the ventricles were eroded to some extent by the tumor tissue, although the invasion was always superficial. The inferior surface of the corpus callosum, however, was more deeply invaded. In some places the upper half of this structure was preserved, and in other regions only a few millimeters remained undamaged. The pineal body was preserved, although it was surrounded by tumor tissue which had extended posteriorly from the third ventricle. The choroid plexus was infiltrated and partly destroyed. The cause of the distention of the ventricular system was not entirely clear, but it seemed probable that there had been partial obstruction of the foramina of the fourth ventricle during life. Some of the enlargement of the ventricles was probably due to the erosive action of the tumor.

Fig. 2 (case 1).—Photomicrograph (× 125) showing tumor tissue spreading over the surface of the ependyma, which is destroyed in places. Glia fibers extend into the tumor from the subependymal tissues. Hematoxylin and eosin stain.

The brain was fixed in dilute formaldehyde. Sections were stained with eosin and hematoxylin and by the Nissl, Cajal and Perdrau methods.

Microscopic examination revealed that the tumor consisted of an unsystematized proliferation of cells, heaped into irregular masses. The ependyma had been almost completely destroyed, and the tumor cells had invaded the tissues beneath to some extent (fig. 2). There was no suggestion of a capsule, and no definite connective tissue stroma was discovered. There was little vascularization. One gained the impression that the tumor was so friable and loosely knit that its cells were constantly becomng detached into the cerebrospinal fluid, in this way forming new deposits in the ventricles. Two types of cells were distinguished: 1. Large, round or polygonal cells, with deeply staining nuclei and scanty cyto-

plasm. Well defined nucleoli were seen in most cells, and mitoses were rare. No fibers or cell processes were demonstrated. These cells were arranged irregularly in clumps or masses (fig. 3). 2. Small cells, about one-fifth the size of the larger cells, with deeply staining nuclei and scarcely any cytoplasm. They showed no nucleoli, but some cells had a few scattered chromatin granules. These cells were observed in thick mantles surrounding the blood vessels and distending the perivascular spaces. Almost all the vessels of medium size were surrounded in this manner (fig. 4). These small cells had infiltrated the tissues surrounding the ventricles, passing inward along the perivascular spaces (fig. 5). In some regions of the subcortical white matter there were small areas of tissue

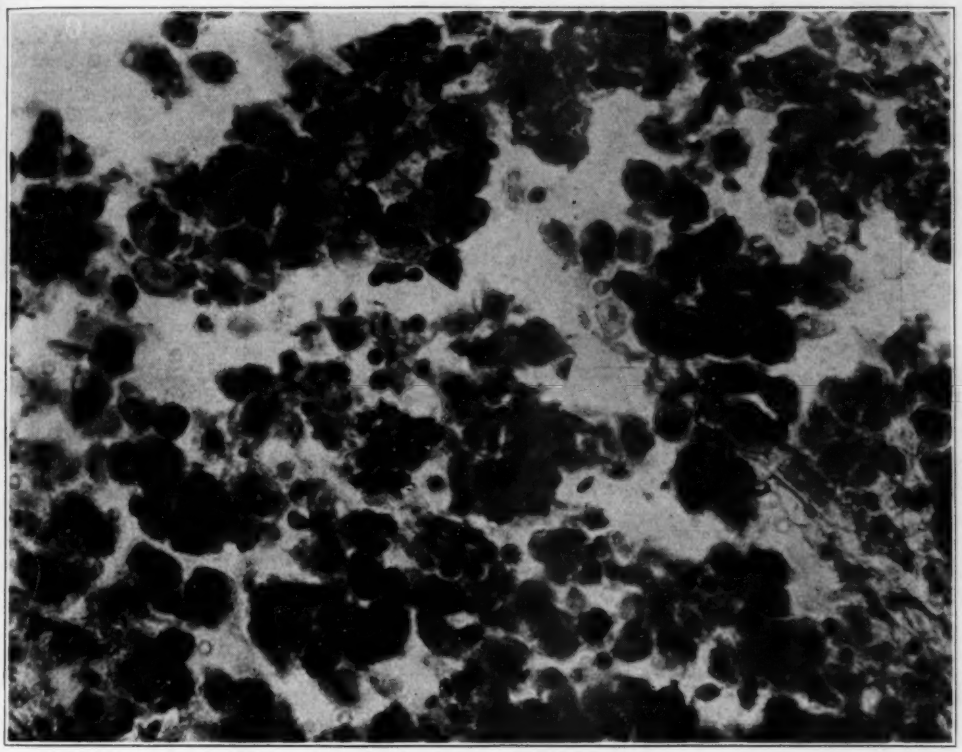

Fig. 3 (case 1).—Photomicrograph (× 500) showing the morphologic character and irregular distribution of the larger cells. Hematoxylin and eosin stain.

destruction remote from the tumor infiltrations and not associated with demonstrable vascular lesions. Such lesions were very small and few. In general the white matter of the cerebral hemispheres was well preserved. No abnormalities were discovered in the cerebral cortex. In several places clumps of five or six of the larger cells were seen floating freely in the subarachnoid space. No metastatic deposits were observed in the meninges, and it was evident that this tumor did not readily form deposits in the meninges, as the medulloblastoma does frequently. Sections of the optic nerve and the retina revealed no atrophy of the optic nerve and no edema.

CASE 2.—*Onset with dulness and forgetfulness. Speech became defective. Polyuria and excessive thirst appeared four years later. Somnolence and fever developed the next year. Soon the gait became unsteady. There was no evidence of increased intracranial pressure. Death five years after onset, with hyperpyrexia. Postmortem examination revealed a small growth arising in the anterior part of the third ventricle and spreading throughout the ventricular system.*

History.—R. T., a man aged 23, began to complain of headache and loss of appetite in 1925. He was dull and apathetic. He consulted a physician because of these symptoms, but nothing abnormal was discovered. Despite the symptoms, he continued to work until February 1929, when an illness diagnosed as influenza kept him in bed for several days. In March he was still vaguely ill. In May

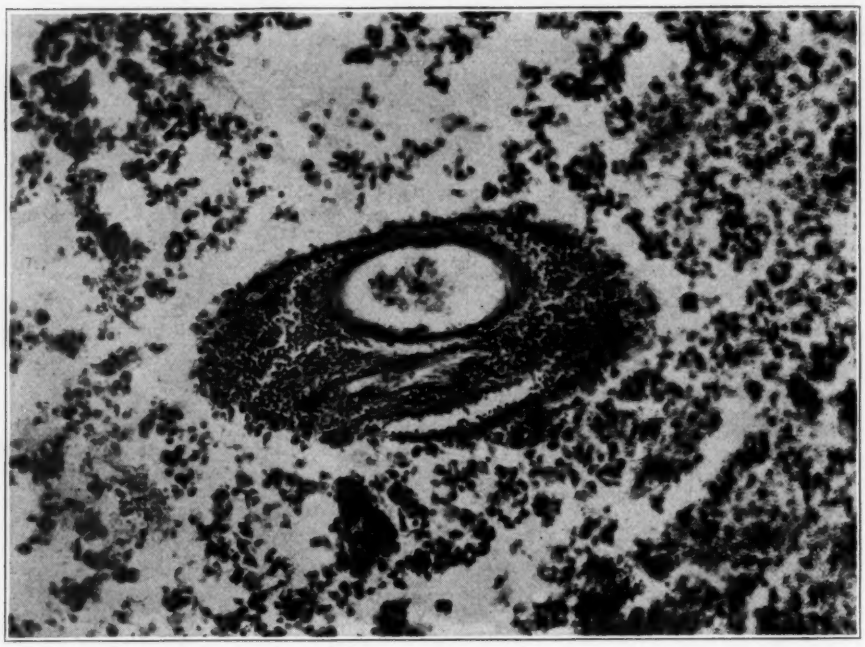

Fig. 4 (case 1).—Photomicrograph (× 125) of a characteristic area of the tumor. A small blood vessel in the center of the field is surrounded by a dense zone of the smaller cells. The larger cells are scattered irregularly over the rest of the field. The absence of stroma is apparent. Hematoxylin and eosin stain.

his gait became unsteady, and he complained of insomnia. There were polyuria and excessive thirst. He began to gain weight rapidly. A second examination failed to discover any definite abnormality, but a diagnosis of thyroid deficiency was made because of a low basal metabolic rate (—30). He was able to work during June and July. In September he was very forgetful and could not remember engagements. In December he worked hard, in a confused way, but accomplished little. Speech was disconnected, and the sentences were incomplete. He stumbled in walking. His mother insisted that he stop work and consult a physician. On December 24 he entered a hospital, where he slept constantly for several

days. The temperature was elevated at times, reaching 101 F. At night he was confused and wandered around the wards. Memory was defective. The spinal fluid is said to have shown no increase in cells and a negative Wassermann reaction. The protein content was not estimated.

Examination.—On Jan. 24, 1930, the patient entered the Henry Phipps Psychiatric Clinic, in a severely dehydrated condition. He was semistuporous, but when aroused was able to converse intelligently, lapsing into sleep when left alone for a moment. He was cheerful and even jocular. Orientation and memory were defective. The cranial nerves were normal. No edema or atrophy of the disks

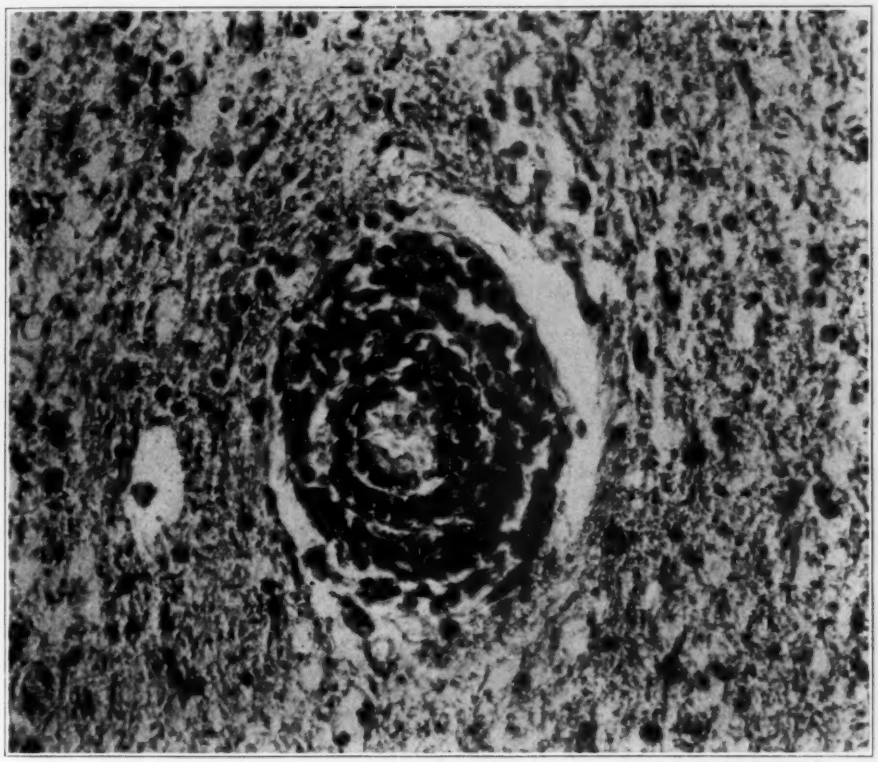

Fig. 5 (case 1).—Photomicrograph (× 500) showing how the tumor cells infiltrate the tissues by way of the perivascular spaces. Hematoxylin and eosin stain.

was apparent. There was slight general increase of the tendon reflexes, but no paralysis, spasticity or ataxia. Speech was indistinct, and the sentences were imperfectly formed. In other respects neurologic examination gave normal results.

The nonprotein nitrogen of the blood was 72 mg. per hundred cubic centimeters. The blood sugar level was normal. The urine contained albumin and casts. The blood pressure was 80 systolic and 55 diastolic. Blood counts and examination of blood smears revealed nothing abnormal. The spinal fluid was not examined.

Course.—On January 27, respiration of the Cheyne-Stokes type and tachycardia developed; the temperature rose to 106.4 F., and the patient died.

Autopsy.—Postmortem examination revealed extensive lobar pneumonia and no other changes in the abdominal or thoracic viscera. The brain was normal externally and showed no signs of increased intracranial pressure. The meninges were delicate. There was mild enlargement of the ventricles. The ventricular system was lined by a soft, spongy tissue, which extended throughout the lateral, third and fourth ventricles, destroying almost the entire ependymal membrane. This tissue seemed to have its origin in a soft mass of tumor in the anterior part of the third ventricle, which had invaded the base of the infundibulum and the anterior part of the hypothalamus and extended into the lateral ventricles by way of the foramina of Monro. The columns of the fornix were partially destroyed, and the under half of the corpus callosum was invaded and softened. The pineal gland was intact and of normal size. The choroid plexus was densely infiltrated by the growth. Histologic examination revealed the same types of cells as those described in the preceding case. The large cells were arranged in irregular masses, but the small cells were observed, for the most part, in the distended adventitial sheaths of the small and medium blood vessels. A few clumps of the larger cells were present in the meninges over the cerebellum and corpora quadrigemina, apparently floating freely in the subarachnoid space. There were no demonstrable lesions in the subcortical white matter or in the cortex. The optic nerves were normal.

CASE 3.—*Failing vision, weakness, drowsiness and vomiting. Forgetfulness and euphoria. Primary atrophy of the optic nerve. The spinal fluid contained 60 cells; the amount of protein was increased. Progressive cachexia, dehydration and stupor. Death a year after the onset. Postmortem examination revealed a small growth arising in the third ventricle and spreading throughout the ventricles.*

History.—S. V., a man aged 21, began to complain of failing vision in the summer of 1927. Soon, he began to vomit and to lose weight rapidly. In the fall and early winter these symptoms continued, and in March he began to be drowsy and to stay in bed most of the time because he was so "weak." He took no interest in work and was forgetful and apathetic. There was no complaint of headache, but vomiting was a constant symptom. On July 27 he was admitted to the Henry Phipps Psychiatric Clinic.

Examination.—The patient was well developed but much emaciated, weighing only 73 pounds (33.1 Kg.). He was dull and slept most of the time. When asked about his mood, he answered that he was quite happy. He seemed to be unconcerned about his condition. Memory was poor, and he was completely disoriented. At times he was querulous and irritable. The pupils were dilated, and the light reflex was diminished. The optic disks were slightly pale but not edematous. Vision was reduced, but he could count fingers. There was some restriction of the temporal fields on both sides. The other cranial nerves were normal. There was no local weakness, spasticity, or ataxia, but strength in general was reduced, apparently owing to the general condition. No changes in sensibility were detected. The knee jerks were greatly reduced or lost, but the other tendon reflexes were normal. The plantar response was of flexor type. There were no signs of meningeal irritation.

Spinal puncture yielded yellow fluid containing 60 cells per cubic millimeter. The protein was greatly increased.

Course.—The patient continued to vomit and to lose weight and strength. There was conspicuous dehydration. The temperature varied from 94 to 102.4 F.

The mood was euphoric. The sensorium became clouded, and stupor supervened. Death occurred during convulsions, on August 30, about one year after the first symptom was noted.

Autopsy.—The body was greatly emaciated, but no evidences of disease were observed outside the nervous system. The brain was normal externally except for the presence of a soft, friable tumor just behind the optic chiasm, in the region of the infundibulum. There was possibly slight flattening of the convolu-

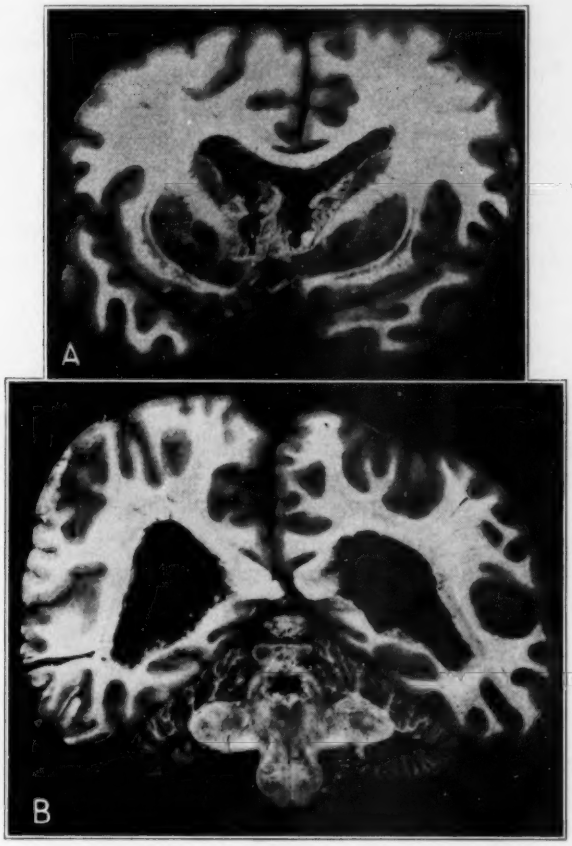

Fig. 6 (case 3).—*A*, section through the cerebral hemispheres, showing distribution of the tumor in the lateral ventricles, and *B*, a more posterior section, showing tumor tissue in the walls of the fourth and lateral ventricles.

tions, as if there had been mild increase in intracranial pressure. The meninges showed no changes. The ventricles were slightly dilated. A small, spongy tumor in the anterior part of the third ventricle had penetrated the floor of the ventricle and destroyed the infundibulum, presenting externally above the sella. The optic chiasm was compressed. The tumor had extended into the lateral and fourth ventricles, just as had the tumors in cases 1 and 2 (fig. 6 *A* and *B*). The ependymal membrane was largely destroyed and replaced by a thin layer of friable tumor tissue. The periventricular tissues were infiltrated to a depth of about

1 cm., and the lower half of the corpus callosum was destroyed, as in the preceding cases. The pineal body was unaltered. Only a few tumor cells were observed in the subarachnoid spaces, and there were no metastatic deposits in the meninges. The tumor showed histologic characteristics identical with those in cases 1 and 2.

COMMENT

We shall consider first the anatomic aspects of the tumors. They arose apparently in each case in the anterior part of the third ventricle, invading the hypothalamus and then extending throughout the ventricular system in a remarkably diffuse fashion, destroying almost the entire ependymal membrane and infiltrating the adjacent brain tissue to a depth of perhaps 1 cm. in places. The entire ventricular system, including the aqueduct and the fourth ventricle, was more or less dilated in all three cases, but there did not seem to be complete obstruction in any case. The tumors were friable and soft and were not encapsulated. There was practically no stroma, and vascularization was scanty. They were composed of cells of two types: large, round or polygonal cells, with deeply staining, round nuclei and large nucleoli, and small cells, with little or no cytoplasm and very dense nuclei. The former were arranged in irregular masses and clumps, and the latter, in thick mantles surrounding the small and medium blood vessels. Few mitoses were seen. The infiltration of the brain was due to penetration of the perivascular spaces by the small cells. A few tumor cells of the larger variety were observed floating in the subarachnoid spaces. These tumors did not metastasize to the meninges, as does the medulloblastoma.

We have been unable to find in standard textbooks of pathology a description which could be applied to the three tumors which form the subject of this paper. A fairly comprehensive survey of the current literature concerned with the histology and classification of neoplasms of the brain has likewise been fruitless. Certain features of the tumors in our cases were observed in a case described by Christin and Naville in 1920.[2] The gross appearance of the tumor in their case was identical with that in our cases. The histologic description, however, revealed several important differences. For example, Christin and Naville observed glia fibers in their case, and some of the large cells showed definite processes and multiple nuclei. Moreover, large cells resembling ganglion cells were present in the tumor. The tumors in our cases showed none of these characteristics. They contained no glia fibers. The large cells exhibited no processes, and none contained more than one nucleus. Ganglion cells were absent. These differences seem to be so definite that we have been led to conclude that the case of Christin and Naville was essentially different from our cases. We have there-

2. Christin, E. C., and Naville, F.: Les tumeurs diffuses des parois ventriculaires (neuroblastomes embryonnaires), Schweiz. Arch. f. Neurol. u. Psychiat. **6**:49, 1920. This reference was furnished us by Dr. Paul Bucy.

fore concluded that it is impossible to identify our tumors with any described in the papers we have consulted.

The cells of the tumors in our cases show no tendency toward differentiation. They present none of the characteristics of cells of the glial series, ependymal cells or primitive nerve cells. We have seen nothing to indicate that the tumors may be sarcomas. The true nature and exact origin must remain uncertain for the present. Since in all three cases the growth seemed to have arisen from the walls of the third ventricle, it may be suspected that it arose from some structure peculiar to that region. A number of vestigial structures are observed in the walls of the third ventricle during embryonic life. These disappear long before birth but may leave cell rests which are capable of giving rise to a tumor. The possibility that the tumors sprang from such embryonic remnants is at least worthy of consideration.

The clinical features in the cases were not less distinctive than the anatomic. The tumors all occurred in young men. The age at the onset of symptoms varied from 15 to 27 years. There were symptoms indicative of increased intracranial pressure, such as headache and vomiting, but never definite papilledema, bradycardia, palsy of the sixth nerve or other evidence of severe elevation of intracranial pressure. In one case there was atrophy of the optic nerve due to direct compression of the chiasm. In all cases there were signs of involvement of the hypothalamus. Somnolence was present in all three cases. Polyuria and polydipsia appeared in two cases and may have been masked by stupor in the third case. Regulation of temperature was affected in all cases, hypothermia being present in two instances and hyperthermia in the third. Sugar metabolism was not altered. None of the patients was obese, but in case 3 there was striking emaciation, which was not adequately explained by the diet. The basal metabolic rate was reduced to —30 in case 2. All the patients showed unsteadiness of gait, and all had disorders of speech, including difficulty in understanding and a tendency to employ words unsuitable for their meaning. In case 1 there was definite motor apraxia during the last few months of life. There was no paralysis, anesthesia or ataxia, and in general neurologic examination yielded few objective signs. Mental changes were prominent in all cases and were such as to require confinement in a psychiatric hospital. There were drowsiness, clouding of consciousness, loss of memory, loss of initiative and mild euphoria which gave way at times to restlessness and irritability. The spinal fluid in two cases showed pleocytosis, with a count of from 60 to 70 cells per cubic millimeter. These cells were reported as lymphocytes, but, since tumor cells, and not lymphocytes, were observed in the meninges, it is probable that they were really tumor cells. In the third case cells would almost certainly have been seen in the spinal fluid if it had been examined, for they were easily observed in the meninges. There was an excess of protein in the spinal

fluid. Ventriculography was performed twice in one case, but the diagnosis was not established by this means, for no definite tumor was visualized.

Correlation of the symptoms with the anatomic changes is not easy. The presence of the growth in the third ventricle, with distention of the ventricle and infiltration of the infundibulum and hypothalamus, offers an adequate explanation for the polyuria, polydipsia, somnolence and loss of temperature regulation. The mild symptoms of increased intracranial pressure were apparently due to partial obstruction of the foramina of the fourth ventricle by bits of tumor tissue, for no complete obstruction was to be demonstrated. The cells in the spinal fluid were evidently neoplastic, for tumor cells were seen floating in the subarachnoid spaces post mortem. The unsteadiness of gait must have been due to increased intracranial pressure and hydrocephalus, for there was no ataxia and no spasticity. The apraxia in case 1 can be explained by destruction of the inferior half of the corpus callosum, and the same explanation may be offered for the mental changes. The disturbances of speech, however, are difficult to understand. There were no lesions in the cerebral cortex or the white matter immediately beneath the cortex. The central white matter in proximity to the ventricles was destroyed to a depth of 1 cm. or more, but one would not have expected aphasia to result from lesions so remote from the cortex.

The diagnosis was not definitely established in any case before postmortem examination. In fact, in one case the gross appearance led the pathologist to make a provisional diagnosis of "ependymitis." Several clinical diagnoses other than that of intracranial tumor were considered in each case. In case 1 the age at onset of 15 years, the signs of diffuse cerebral damage, the mild evidences of increased intracranial pressure, the ventriculographic findings, which were regarded as excluding tumor, and the moderate pleocytosis in the spinal fluid led to a provisional diagnosis of Schilder's encephalitis periaxialis diffusa. In case 2 the diagnosis of epidemic encephalitis was seriously considered because of the fever and prolonged somnolence. In case 3 a diagnosis of suprasellar tumor was made because of the primary atrophy of the optic nerve and the somnolence.

A growth of this type is obviously inoperable from the beginning. In case 1 a remission of two years followed exploration of the posterior fossa and postoperative irradiation; so it is possible that the tumor may be influenced favorably by radiation.

SUMMARY AND CONCLUSIONS

1. Three cases of malignant tumor of the third ventricle are reported in which we are unable to identify the growth with any tumor described previously.

2. The tumors arose in the anterior part of the third ventricle and extended throughout the ventricular system, destroying the ependyma and infiltrating the brain to a variable depth. They did not extend into the meninges.

3. The tumors were composed of cells of two types: (1) large, round or polygonal cells, with deeply staining, round nuclei and large nucleoli, which were arranged irregularly in clumps and masses, and (2) small cells, with little or no cytoplasm and small, deeply staining nuclei, which were seen in thick mantles surrounding the small and medium blood vessels.

4. The clinical features included mild symptoms of increased intracranial pressure, such as headache and vomiting, but never definite, outspoken papilledema, bradycardia or palsy of the sixth nerves.

5. In all three cases there were definite signs of involvement of the hypothalamus, including pronounced somnolence, polyuria and disturbances in temperature regulation.

6. In one case there was primary atrophy of the optic nerve due to direct compression of the chiasm.

7. The gait was unsteady in all cases.

8. There was disorder of speech resembling paraphasia in all three cases, and in one case there were alexia and apraxia.

9. Mental disturbances were invariably present. There were clouding of consciousness, loss of memory, loss of initiative, mild euphoria and, at times, restlessness and irritability.

10. The spinal fluid showed pleocytosis, with a count of between 60 and 70 cells, and excess of protein in two cases. The spinal fluid was not examined in the third case.

11. Ventriculography was performed twice in one case, but no tumor was visualized.

12. The ages of the patients at the onset of symptoms ranged from 15 to 27 years.

13. The duration of the course varied from one to five years.

14. A diagnosis of intracranial tumor was never definitely established before postmortem examination in any of the cases. In addition to tumor of the brain, the diagnosis of Schilder's encephalitis periaxialis diffusa and epidemic encephalitis were considered in cases 1 and 2, respectively, and in case 3 the diagnosis of suprasellar tumor was made because of atrophy of the optic nerve.

Miss Cecilia Bisson made the illustrations.

ELECTRO-ENCEPHALOGRAPHY

III. NORMAL DIFFERENTIATION OF OCCIPITAL AND PRECENTRAL REGIONS IN MAN

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The present paper is concerned with the bio-electric activity of the precentral and occipital cortical fields in man as recorded from the surface of the head.

Berger,[1] in a series of carefully controlled studies, has shown that changes in potential of brain origin can be recorded from the surface of the head in man. He observed that these changes in potential are detectable from various regions of the head, since they are obtained when almost any part of the surface is included between two electrodes adequately separated. Furthermore, it appeared from his records that regular rhythms of the same frequency (the 10 cycle alpha rhythm and the beta rhythms of from 25 to 50 per second) are obtained simultaneously from various parts of the head in normal persons; he therefore concluded that the entire brain or any particular region presents one type of bio-electric activity.

Tönnies,[2] Adrian and Matthews [3] (page 355) and Adrian and Yamagiwa [4] concluded from their experiments that the alpha rhythm, although it can be detected from almost any part of the head, appears to have its origin in the occipital region. This is in harmony with the common observation that the occipital alpha rhythm is usually readily affected (either abolished or controlled in frequency) by visual stimulation. All potential gradients in the scalp were considered by these authors to be due mainly, at least, to the activity of the occipital lobes.

From the Emma Pendleton Bradley Home and Brown University.

1. Berger, H.: (*a*) Ueber das Elektrenkephalogramm des Menschen, Arch. f. Psychiat. **87**:527-570, 1929; **94**:16-60, 1931; **97**:6-26, 1932; **98**:231-254, 1933; **99**:555-574, 1933; **100**:301-320, 1933; **101**:452-469, 1933; **102**:538-557, 1934; **103**:444-454, 1935; **104**:678-689, 1936; (*b*) Ueber das Elektrenkephalogramm des Menschen, J. f. Psychol. u. Neurol. **40**:160-179, 1930.

2. Tönnies, J. F.: Die Ableitung biolektrischer Effekte vom uneröffneten Schädel, J. f. Psychol. u. Neurol. **45**:154-171, 1933.

3. Adrian, E. D., and Matthews, B. H. C.: The Berger Rhythm: Potential Changes from the Occipital Lobes in Man, Brain **57**:355-384, 1934.

4. Adrian, E. D., and Yamagiwa, K.: The Origin of the Berger Rhythm, Brain **58**:323-351, 1935.

Adrian and Yamagiwa stated that under abnormal conditions other regions of the brain may be set into synchronous discharge so as to produce potentials of sufficient magnitude to be detected on the surface of the head but that in the normal conscious subject the only potentials detectable from the surface arise from the occipital lobes. Consequently, it has been suggested that the term "Berger rhythm" be applied to the 10 cycle rhythmic potentials in place of the term "electro-encephalogram," as suggested by Berger, since the latter term implied that the potentials observed might originate from any part of the cerebral cortex. We have obtained evidence which we interpret in favor of Berger's conclusion, namely, that disturbance in rhythmic potentials from regions of the brain other than the occipital may be detected from the surface of the head; therefore we believe that the original term suggested by Berger should be retained and that such records should be called electro-encephalograms.

As we have pointed out in a previous publication,[5] detection of the same rhythm of potential change from different regions of the head does not make it easy to determine whether these potentials have a common source or many sources, since the response of various cortical regions may be physiologically linked in such manner as to cause them to beat at the same frequency. If, however, one is able to record different frequencies and types of potential change from different regions, one has the proof not only that there is independence of recording from the purely electrical point of view but that various regions of the brain in the normal conscious subject may produce rhythmic potentials of sufficient magnitude for detection on the surface of the head.

METHOD

The subjects used in the present study were placed in semireclining or reclining position in a sound-resitant, electrically shielded room. The recording apparatus was in adjoining shielded rooms, so that the subject was undisturbed during the experiment except for the light and sound stimuli controlled from the recording rooms.

The amplifiers consisted of four completely independent push-pull four stage units with separate plate supplies, so as to insure independent differential recording from four pairs of electrodes, no electrode being directly grounded. Two microfarad condensers and 0.5 megohm grid resistors were used in the resistance-capacity coupling. A Westinghouse type PA, four element oscillograph with a natural frequency of 1,500 cycles was used in recording.

The electrodes consisted of small chlorided silver hats with felt-covered brims, which had an inside diameter of 5 mm. Each electrode was fixed to the head with collodion, the contact with the scalp being made through electrode jelly. The lead wires from the head to the amplifiers were about 3 feet (76.2 cm.) in

5. Jasper, H. H., and Andrews, H. L.: Human Brain Rhythms: I. Recording Techniques and Preliminary Results, J. Gen. Psychol. **14**:98-126, 1936.

length. The type of electrode previously described [5] was used for some of the early records but was abandoned because of the greater convenience of the type described here.

We found in our previous studies that the electro-encephalogram may be simplified in many cases when the two electrodes are placed over a more or less homogeneous cortical field. Furthermore, differential recording from various parts of the head is also greatly improved by this method as compared with the results obtained by methods which involve the placing of electrodes so as to include a large portion of the head between them. Most placements of electrodes used in the present study were determined by a set of standard positions worked out for the purpose of getting a pair of electrodes as close together as possible on the surface of the head over a given cortical field, as determined from the topographic landmarks and measurements used in operations on the brain and from roentgenographic studies of the skulls of some of our subjects.

The placements of pairs of electrodes for recording from the frontal, precentral, parietal, occipital and temporal regions of the brain are given in figure 1. Records taken with the paired placements were always checked by recording also from one of the pairs to a common, more diffuse lead taken from the lobes of the two ears, even though one cannot obtain, except under special conditions, as good localization by the latter method. The method of localization from phase relations between successive pairs in a line of electrodes was also used [5] in the work preliminary to this study.

We are at present conducting a complete study of the normal electro-encephalogram obtained with each of the standard electrode placements, recording, in different combinations, simultaneously from four regions. Since we have made a more intensive study of the precentral and occipital regions, the records which showed a satisfactory simultaneous comparison of these two regions have been used in the present report. This selection was made to demonstrate that a real differentiation is possible from the surface of the head in the normal subject and also to show some of the characteristics of the precentral beta potentials as compared with those of the occipital alpha potentials. Records from one hundred experiments carried out over a period of eighteen months on thirty-four subjects, seventeen men and seventeen women, form the data which have been analyzed for this discussion. The subjects were chiefly members of the hospital staff and graduate students of Brown University, whose ages ranged from 20 to 50.

RESULTS

The Alpha Rhythms.—Adrian and Yamagiwa presented a rather convincing argument for the occipital origin of the 10 cycle rhythm, on the basis both of its relation to visual stimulation and of phase reversals. Phase reversals in a line of four or five electrodes spaced 15 mm. apart gave results in persons with large occipital alpha potentials which could be interpreted according to the conception of Adrian and Yamagiwa, namely, that these potentials had a single source in the occipital lobe. In other normal persons, however, the results were contrary to this interpretation and could be explained only on the basis of there being many groups of cells in various regions of the cortex which generate sufficient disturbance of potentials for detection on the surface of the head.

The alpha rhythm of Berger (from 8 to 12 per second), together with components of higher frequency (the beta rhythms), was observed from a pair of electrodes over the precentral region. The alpha rhythm from this region showed certain characteristics which indicate a cortical origin independent of that of the occipital alpha rhythm, so that we have called it the precentral alpha, as opposed to the occipital alpha, phenomenon. These characteristics may be summarized as follows:

1. The spontaneous disappearance and appearance of alpha potentials recorded from over the occipital region do not correspond to these variations obtained from over the precentral region.

2. Stimulation with light, under certain conditions, may block the occipital alpha potentials while simultaneously causing no effect on, or even facilitating, the precentral alpha potentials.

3. In one normal adult subject (H. A.) we found the precentral alpha potentials to be consistently of greater amplitude and regularity than the occipital alpha potentials.[6] Thirteen records taken on this subject over a period of eighteen months revealed considerable variability from day to day; all agreed, however, in showing predominance of alpha potentials from the precentral region, even though under certain conditions the occipital alpha potentials could be observed for a short period at an amplitude and regularity equal to those of the precentral alpha potentials (fig. 2).

4. Frequencies observed from the precentral region may differ from those taken simultaneously from the occipital region. This difference usually consists in a greater proportion of the higher frequencies in the precentral region (fig. 3), but occasionally (in about 5 per cent of subjects) one may observe a greater proportion of low frequencies in the precentral and frontal regions than in the occiput. Also, the occipital alpha frequently may be different from the precentral alpha frequency in some subjects.

The Beta Rhythms.—Berger found in his records taken with the entire head included between two electrodes that there is always a secondary rhythm or rhythms superimposed on the alpha rhythm, which he called the beta waves. These waves appear at frequencies of from 20 to 50 per second. Adrian and Yamagiwa expressed the opinion that the little irregularities superimposed on the large alpha rhythms were

6. These results have been checked with records taken from a diffuse lead to the occiput and the precentral regions, with essentially the same results, so that the absence of the occipital alpha rhythm cannot be due to the paired method of recording. A complete roentgenographic study of the skull of this subject, as compared with similar studies on subjects presenting predominant occipital alpha potentials, showed no differences in thickness or formation of bone which could account for the marked difference in the electro-encephalogram.

EXPLANATION OF FIGURE 1

Fig. 1.—Standard electrode placements. *A* is a photograph of a full size plaster model of the human head (reduced about one half), with markings which indicate roughly the location of underlying cortical areas. The electrodes used for recording from the frontal, precentral, parietal, occipital and temporal regions, including the diffuse lead from the ear, have been attached exactly as they are used in all our studies. In *B* measurements for placement of pairs of electrodes along the median sagittal line are made to the transverse plane of the median electrodes. Position I (frontal) lies one-half the distance from the glabella to the midsagittal point; position II (precentral), in a line drawn from the midsagittal point to the center of the zygomatic arch; position III (parietal), one-half the distance from the lambda to the midsagittal point; position IV (occipital), one-fourth the distance from the lambda to the inion, and position V (temporal), on a line drawn from the auricular to the midsagittal point, about 1 cm. below the temporoparietal suture. The inside separation of all pairs of electrodes equals 20 mm. The median electrode on one side is separated from that of the homologous pair on the other side by a distance of 3 cm., i. e., 15 mm. on either side of the midline.

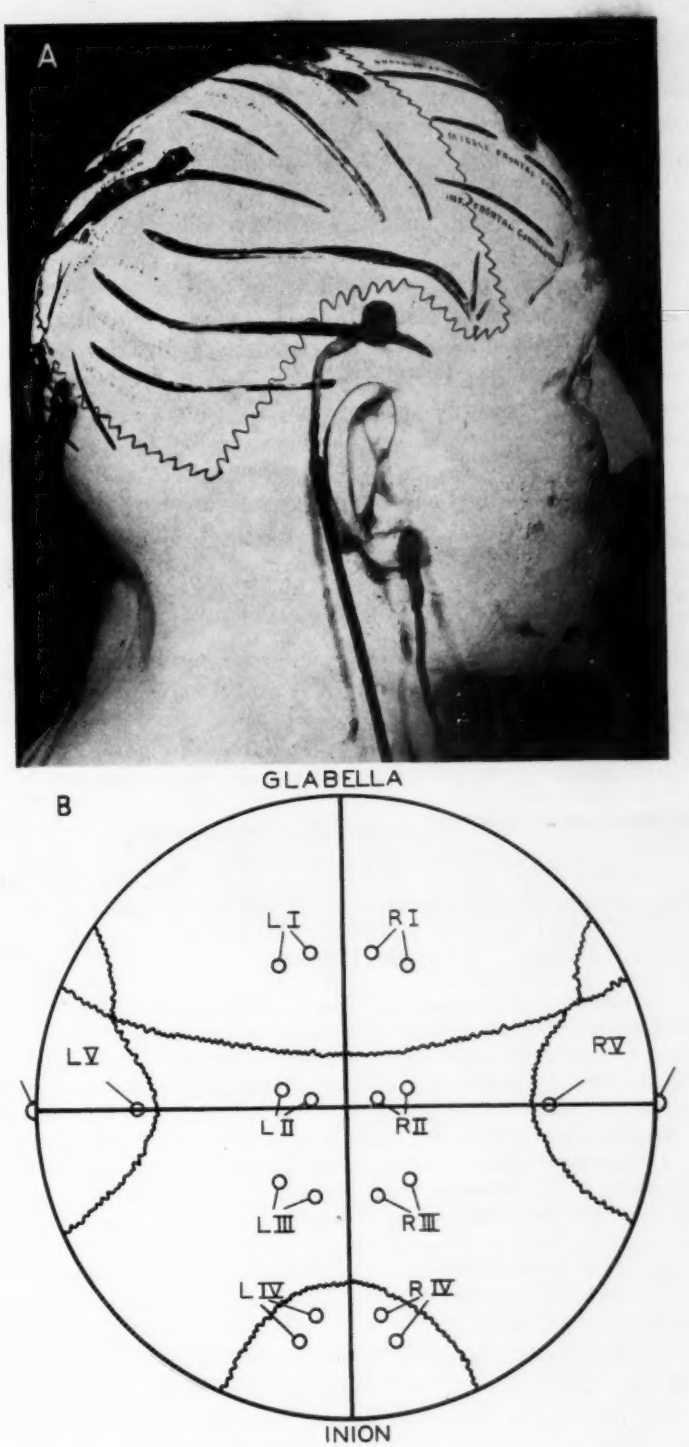

Figure 1

of muscular origin or were due to inflections of the alpha potentials analogous to those observed in the heart.

We have shown in a previous publication [5] that in most persons the beta waves appear to predominate in the precentral region of the head and that in some subjects, under the proper conditions of relaxation, one can obtain regular rhythmic potentials at about 25 cycles per second from the precentral region, while recording at the same time smooth, regular alpha potentials at about 10 cycles per second from the occiput. In most persons there are potentials from the precentral region at 10 a second, the precentral alpha rhythm, as well as the precentral beta rhythms, at from 18 to 30 per second. Also, one often finds a faint, and occasionally a clear, beta rhythm superimposed on the alpha poten-

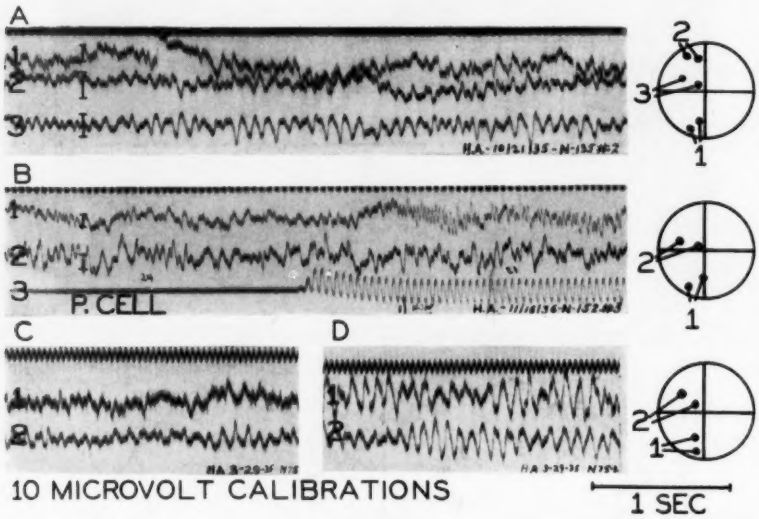

Fig. 2 (subject H. A.).—*A*, simultaneous occipital, precentral and frontal records from paired electrodes, as indicated, showing predominance of alpha rhythms, with some beta rhythm in the precentral region. *B*, records taken from the same subject on another day, showing absence of occipital alpha potentials with occipital potentials following at double the frequency of a light flickering at 20 per second as indicated by the signal from a photo-electric cell (lower line). *C* and *D* represent occipital and precentral potentials preceding and following stimulation with light. Occipital alpha potentials are practically absent preceding stimulation but are enhanced to equal the size of the precentral alpha potentials after stimulation, showing that the occipital region in this subject is capable of producing a good alpha rhythm but that this rhythm is characteristically more prominent in the precentral region.

tials from the occipital region. This rhythm we have termed the occipital beta rhythm. We believe these rhythms to be distinct and referable to a particular region, when the proper precautions are taken to lead off from that region by means of a pair of electrodes placed close

together (from 15 to 25 mm.) and when relative amplitudes are given proper consideration.[7]

Since the beta potentials from the precentral region are, on the average, only about one-half the magnitude of the alpha potentials and since they have not received as much attention as the occipital alpha potentials, we shall summarize the evidence which indicates that these potentials are of cerebral origin and have characteristics which suggest that they may originate in cortical regions functionally and anatomically distinct from those giving rise to the occipital alpha potentials.

1. Predominance in the Precentral Region: The beta rhythm from the precentral region may predominate in some subjects to the extent that one rarely sees any alpha rhythm from this region, even though at the same time regular alpha potentials are recorded from the occipital leads (fig. 4). In the majority of subjects one finds both alpha and beta potentials from the precentral region, but a greater proportion of beta potentials in the precentral than in the occipital region (fig. 3). In 12 per cent of our subjects we found little alpha rhythm from either the occipital or the precentral region, a beta rhythm being predominant in both areas but not at the same frequency. Curiously, all these subjects were women.

2. Regularity: To assure accuracy of measurement and a definite frequency, we considered a series of potentials as a definite rhythm only when it was composed of at least 5 successive waves separated by approximately equal periods. The successive periods of the beta rhythm are often as regular as those of the occipital alpha rhythm (fig. 4 *E*). In other records a great deal of irregularity exists in both the alpha and the beta potentials, making measurements of frequency difficult. In some of these records this irregularity is due to still higher frequencies present simultaneously with the alpha and beta frequencies, which serve to complicate considerably the interpretation of the records. These higher frequencies (from 35 to 45 per second, which might be called gamma waves) have not as yet been observed with sufficient regularity for analysis.

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7. The studies of Adrian and Yamagiwa have shown that alpha potentials recorded from a pair of electrodes on the vertex in some subjects appear to originate from a single source in the occiput, owing to their phase relations with alpha potentials recorded simultaneously from a pair of electrodes in the same plane on the occiput. Consequently, the appearance of alpha potentials from over the precentral region does not assure their origin in this region. From consideration of the attenuation which must result from conduction of potentials from the occipital to the precentral pair of electrodes as they are placed in our experiments, we have assumed that alpha potentials from the precentral region, which are from two-thirds to twice the magnitude of similar potentials simultaneously recorded from the occiput, must have origin more nearly beneath the precentral than the occipital pair of electrodes. A full discussion of all factors involved in a "proper" consideration of relative magnitudes (such as attenuation resulting from a focus of activity lying between the two electrodes) cannot be given at this time. This is a complicated question. We have not been able to base regional differentiation on relative amplitudes alone. It has been determined chiefly by differences in composition of frequencies and by differential response to stimulation.

3. Frequency: Measurements of frequency were made only on regular groups of from five to ten waves for both the alpha and the beta rhythms. A series of ten waves was used, except in groups in which it was impossible to obtain as long a series as this without including one or two irregular periods which would tend to give erroneous measurements of frequency. At least ten such groups were measured at random intervals throughout the record for most subjects, so that a sampling of about one hundred regular potentials was included in each determination of average frequency. We found that this method of sampling yielded average values not significantly different from a much larger number of measurements, if

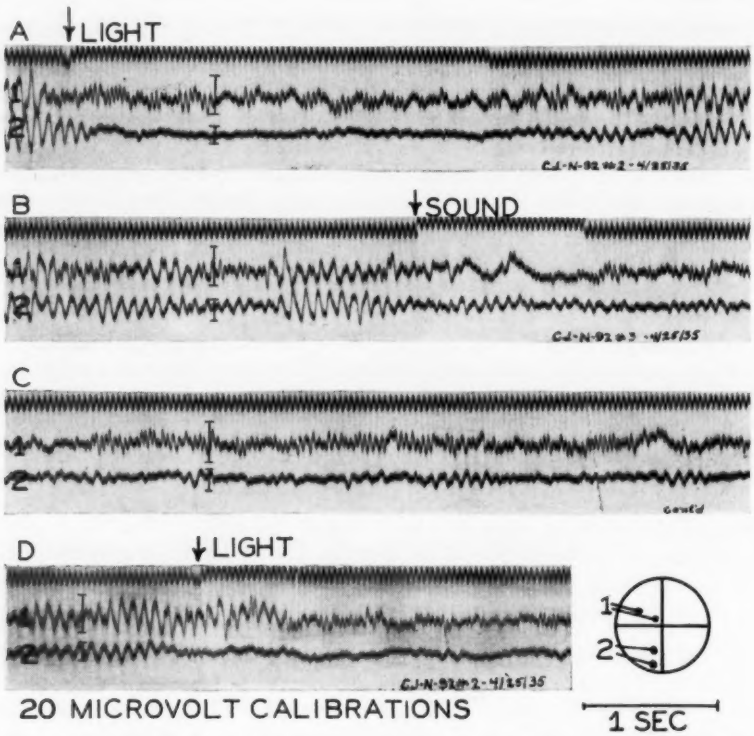

Fig. 3 (subject C. J.).—*1*, the precentral, and *2*, the occipital, record from pairs of electrodes, as indicated. *A* shows blocking of precentral and occipital alpha potentials by stimulation with light, which is not simultaneous; *B*, blocking of precentral alpha and beta potentials with intense auditory stimulation (500 cycles, at 84 decibels), with partial blocking of occipital alpha potentials; *C*, continuation of *B*, showing return of the precentral beta potentials before that of the occipital alpha potentials, and *D*, persistence of precentral alpha potentials after blocking of occipital alpha potentials.

experimental conditions were maintained constant throughout. Records taken immediately after stimulation were not used, since this may alter the frequencies during rest. The average simultaneous occipital alpha and precentral beta frequencies from records for thirty-four subjects are presented in table 1.

The precentral beta potential appears at a definite frequency of about 25 per second. There is a little more variability from the mean in the distribution of average beta frequencies than in that of the average alpha frequencies (the coefficients of variation being 7.6 and 4.7, respectively), some of which is undoubtedly due to greater errors of measurement in determinations of the beta frequencies.

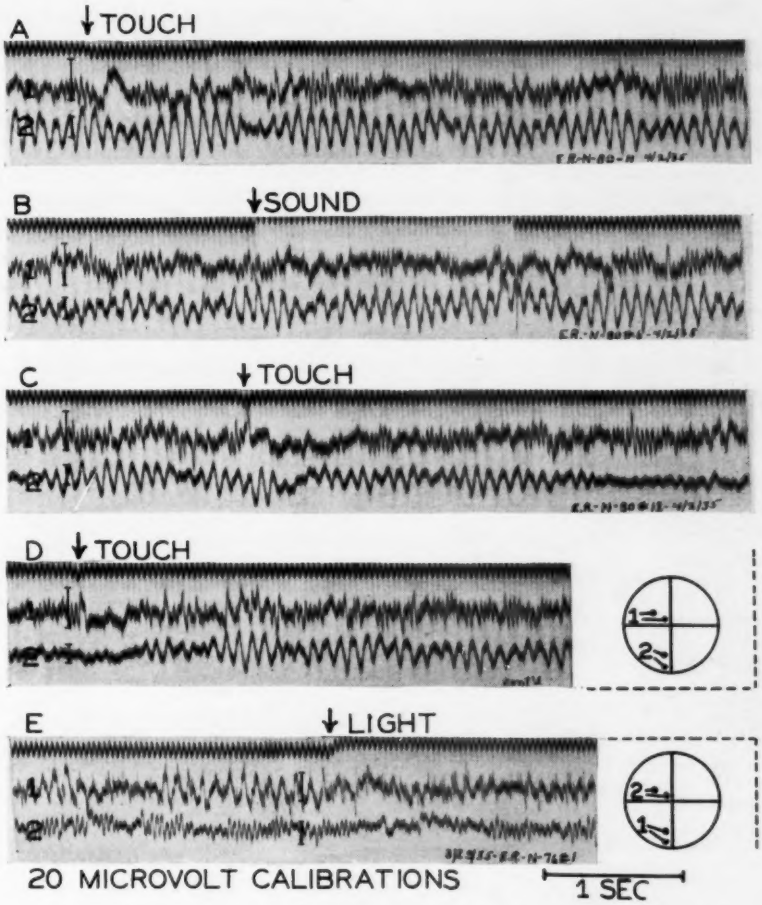

Fig. 4 (subject E. R.).—Precentral and occipital records. *A*, *C* and *D* show blocking of precentral beta potentials with tactual stimulation; *B* illustrates blocking of precentral beta potentials, with no effect on the occipital record from auditory stimulation, and *E*, blocking of precentral beta potentials with intense visual stimulation.

The average alpha frequency for the seventeen men in this group was 10.4, as compared with that of 10.8 for the women. The average beta frequency for the men was 24.2, as compared with that of 25.8 for the women. This suggests a slight tendency to more rapid frequencies in the women, but the differences are not statistically significant in this group of subjects.

4. Amplitude: The amplitude of the beta potentials from the paired leads may vary from 5 to 20 microvolts in different persons. These potentials usually appear at a maximum amplitude of from 10 to 12 microvolts. The amplitude of the alpha potentials recorded simultaneously was found in different subjects to be from one to six times that of the beta potentials. The beta potentials appear most commonly at from one-half to one-third the amplitude of the occipital alpha potentials.

5. Reliability: Measurements were repeated on fourteen of the thirty-four persons at intervals varying from one to eighteen months. On some subjects

TABLE 1.—*Occipital Alpha and Precentral Beta Frequencies in Thirty-Four Subjects*

	Alpha Frequencies		Beta Frequencies	
Record No.	Mean	Range	Mean	Range
N-77	12.4	11.8-15.3	24.4	18.0-28.0
N-105	12.0	11.0-12.5	28.6	23.4-32.6
N-137	11.6	11.4-11.8	19.2	
N-47	11.6	9.8-13.5	25 2	17.8-31.8
N-197	11.6	11.1-12.1	24.0	22.0-25.0
N-45	11.5	10.2-12.5	21.0	18.0-23.8
N-107	11.5	10.8-11.9	28.4	24.8-31.5
N-192	11.4	10.8-11.9	28.2	26.2-30.2
N-219	11.0	10.3-11.5	28.4	27.0-29.5
N-183	11.0	9.1-12.9	26.0	23.0-28.5
N-189	11.0	10.3-12.0	25.8	22.5-30.0
N-205	10.9	10.3-11.7	26.5	24.0-31.0
N-191	10.9	9.9-12.2	25.2	24.2-28.8
N-81	10.8	10.5-11.3	30.8	28 6-33.0
N-172	10.7	10.0-11.3	25.6	22.0-28.0
N-99	10.6	9.3-10.0	25.4	19.7-27.8
N-166	10.5	10.3-11.1	27.5	26.2-29.0
N-180	10.5	10.2-11.0	23.1	22.0-24.0
N-199	10.5	9.5-11.0	21.6	19.0-25.0
N-139	10.4	8.8-12.5	21.2	17.4-28.4
N-202	10.3	9.8-10.9	24.3	23.0-27.0
N-167	10.2	9.6-10.8	26.0	22.0-28.6
N-185	10.2	9.7-11.5	23.6	18.5-28.4
N-213	10.0	9.9-10.3	25.3	23.0-27.0
N-190	10.0	9.5-11.2	27.6	22 0-32.0
N-178	9.9	9.5-10.3	24.2	22.0-25.7
N-94	9.9	9.5-10.6	29.6	26.0-34.0
N-188	9 9	9.3-11.0	22.3	17.0-29.0
N-218	9.8	9.0-10.8	20.4	19.0-24.0
N-155	9.8	9.2-10.6	25.1	25.0-25.1
N-174	9.6	8.0-10.9	20.9	18.5-25.0
N-126	9.5	.....	19.8	16.8-31.6
N-169	9.3	9.0- 9.7	26.5	25.5-28.0
N-177	9.0	7.6-10.3	25.9	24.0-27.6
Mean	10.6 ± 0.1		24.9 ± 0.3	
Probable error	0.5		1.9	

measurements were repeated thirteen or fourteen times during the eighteen months. Occipital alpha potentials are remarkably constant for a given person over long periods, if precautions are taken to maintain the same psychologic and physical conditions of the experiments. Variations in average frequency of only 1 or 2 per cent were observed in six persons, the intervals between measurements ranging from six to eighteen months. Variations in the average frequency of the precentral beta potentials in the same persons were from 2 to 10 per cent, with an average variation of about 5 per cent. Nine (64 per cent) of these subjects showed variations in alpha frequency of not more than 5 per cent, while eight (57 per cent) showed variations in beta frequency of not more than 5 per cent. On the other hand, variations in average alpha frequency of as high as 33 per cent have been observed, but these could usually be accounted for on the basis of known variations in experimental conditions. Variations of from 15 to 27 per cent were also observed

in the beta frequencies, but these were always associated with a variation in alpha frequency in the same direction (although not necessarily of the same amount). Four of the five subjects who had variations in alpha frequency of more than 5 per cent showed also a significant change in beta frequency in the same direction. The average percentage of variation in alpha frequency for this group was 6.8 per cent, while that in beta frequency was 9.5 per cent. In view of the fact that the beta frequencies show greater errors of measurement, it is probable that they are about as constant as the occipital alpha frequencies.

6. Characteristic Variations with Temperature: Changes in frequency of both the occipital alpha and the precentral beta potentials with variation in body temperature were determined in three subjects in whom fever was induced by administration of typhoid vaccine. The variations in average frequencies are shown in table 2.

The course of changes in frequency of the alpha and beta rhythms with variations in temperature and pulse rate in one experiment (subject H. J.) are shown graphically in figure 5. Each point on the curve represents an average value derived from ten determinations (from five to ten waves each). Although

TABLE 2.—*Variations in Brain Rhythms with Changes in Temperature*

Subject	Temperature (Rectal), Degrees Fahrenheit	Occipital Region	Percentage Increase	Precentral Region	Percentage Increase
M. M.	100.0	9.8		27.4	
	104.8	11.0	12	30.9	13
J. H.	98.6	8.9		27.2	
	104.9	10.7	20	31.7	17
H. J.	99.0	10.1		27.6	
	103.0	11.1	11	33.3	12

the percentage change with temperature is roughly the same for both the alpha and the beta phenomenon, there is sufficient discrepancy in the course of the variation to suggest that different cortical cells may be involved.

7. Normal Variations with General Excitatory State: Changes in the general excitatory state of a waking subject, such as occur in drowsiness, tend to change the frequency of both the occipital alpha and the precentral beta potentials. For example, one person at the beginning of the experiment presented a regular occipital alpha potential, at 11 per second, and a precentral beta potential, at 28.6 per second. After one-half hour's experimentation with practically no stimulation, the occipital alpha frequency dropped to 9.5 per second, and the precentral beta frequency, to 25 per second. After the subject was aroused by stimulation with a bright light, the occipital alpha frequency increased to 11.1 per second, and the precentral beta frequency, to 28 per second. The two frequencies do not always have the same percentage variation, nor do they always vary under the same conditions, as is shown by the fact that in some instances the occipital alpha frequency will be increased slightly after stimulation with light, with no apparent effect on the precentral beta frequency.

8. Sleep: Loomis, Harvey and Hobart [8] reported a frequency of 14 per second, which they called the sleep rhythm. They stated that it is usually seen most clearly

8. Loomis, A. L.; Harvey, E. N., and Hobart, G.: Potential Rhythms of the Cerebral Cortex During Sleep, Science **81**:597-598 (June 14) 1935; Further Observations on the Potential Rhythms of the Cerebral Cortex During Sleep, ibid. **82**:198-200 (Aug. 30) 1935.

from an electrode over the vertex. It occurred to us that this 14 cycle rhythm might conceivably be a further decrease in the beta frequency during sleep, since we had observed slowing of the precentral beta frequency in drowsiness. To test this hypothesis, simultaneous precentral and occipital records were taken before, during and after a period of sleep on six normal adult subjects and a child aged

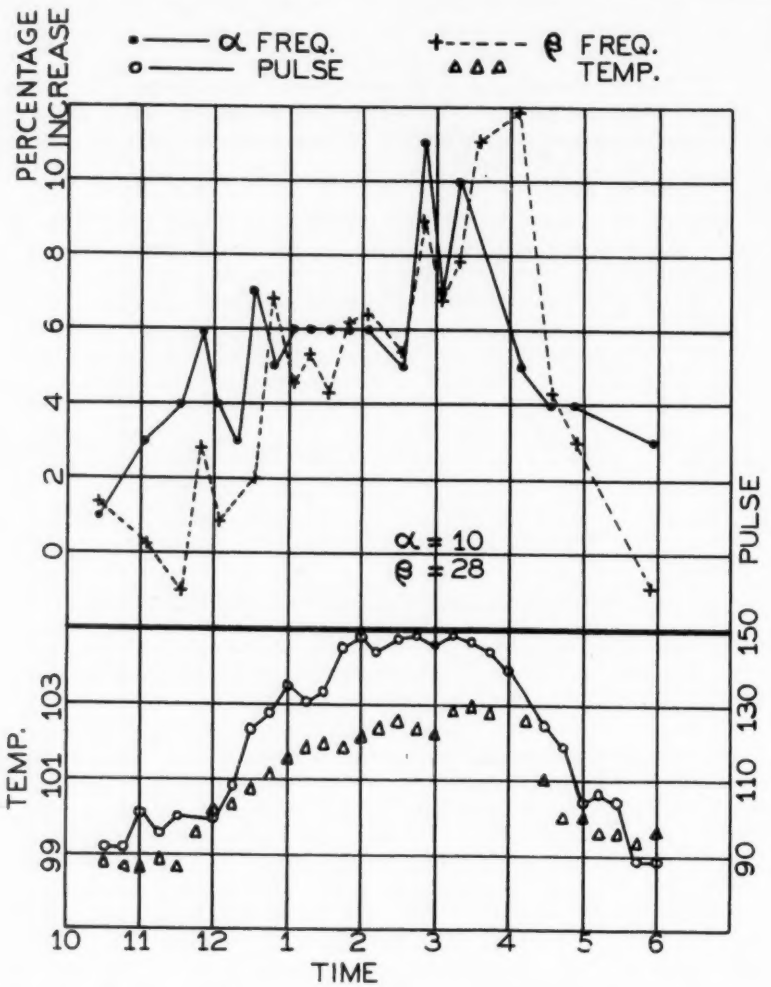

Fig. 5.—Changes in frequency with temperature. In the upper graph changes in occipital alpha frequency as a function of temperature plotted against time (expressed in hours) are shown by the solid line. Concomitant changes in precentral beta frequency are indicated by the broken line. The pulse and temperature readings are indicated in the lower graph.

7 years who was subject to petit mal attacks. The records in figure 6 illustrate the marked effect of sleep on the electro-encephalogram in one of these subjects. These records are not to be considered representative of all persons or of all

stages of sleep, since great individual differences and variations are observed during the course of sleep. The records chosen show, with a clear precentral beta rhythm, the typical changes during from the first half-hour to the first hour of sleep in the absence of any form of external stimulation.

In addition to the fact that the 14 cycle rhythm of sleep appears most clearly from the region of the central fissure in persons who present in the waking state predominance of the alpha rhythm from the occiput and of the beta rhythm from the

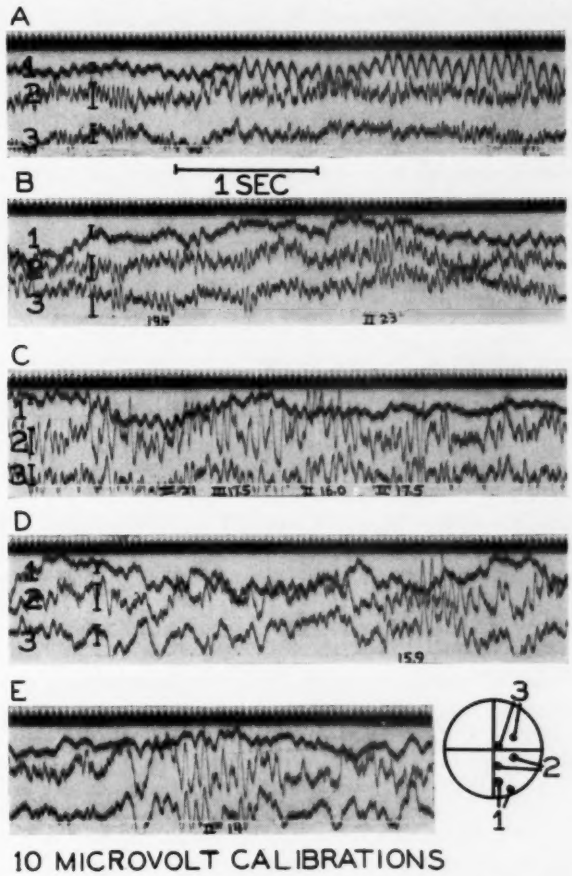

Fig. 6 (subject E. R.).—Precentral, parietal and occipital records taken while the subject was going to sleep. From the record for waking in *A*, to that for light sleep, in *E*, note the progressive changes in frequency of the precentral beta rhythms, the frequencies passing from 29, in record *A*, through 23, 21, 17 and 16 in records *B*, *C* and *D*, to 14, in record *E*.

precentral region, there seems to be a progressive change in frequency from that of the normal precentral beta to the 14 cycle rhythm during transition from the waking to the sleep state. The 14 cycle rhythm occurs only in brief bursts in light sleep and may drop out in deep sleep. It may be much less regular and continuous than the beta waves observed in the waking subject. Much slower, more or less random, potentials occur between the bursts of 14 cycle rhythms.

The electro-encephalogram from the occiput in sleep shows a rapid change to relatively large, slow oscillations. Occasionally these occur regularly enough for a reliable determination of frequency (from 5 to 10 equal periods between waves). These frequencies which appear to range from 3 to 6 or 7 a second, we assume to be the slow alpha waves. Persons with a clear occipital beta wave in the waking state may also show some bursts of 14 cycle frequency of occipital origin in sleep.

9. Relations Between Alpha and Beta Frequencies: We have mentioned some conditions under which the alpha and the beta frequencies appear to increase and decrease together, even though they do not always change to the same degree, and not always simultaneously. It is apparent from table 1 that the absolute values for the occipital alpha frequency do not bear a constant relation to those for the precentral beta frequency. The coefficient of correlation between the two frequencies (product-moment) in the thirty-four cases recorded in this table is 0.22 ± 0.10, which is an almost negligible relationship. It is also important to note that the average precentral beta frequency is not an even multiple of the occipital alpha frequency, as one might expect if the one were derived from the other by a process of multiplication due to inflections of the alpha potentials.

10. Response to Afferent Stimuli: In subjects who present a precentral electro-encephalogram of sufficient regularity and amplitude and one which is relatively free from alpha potentials, it is possible to test the effect of various types of afferent stimuli on the beta rhythm.

Visual, auditory and tactual stimuli of sufficient intensity to produce a definite reflex response (startle) will block both the occipital alpha and the precentral beta potentials, but the latency and duration of the blocked period are different for the two rhythms. A loud noise (e. g., an unexpected 500 cycle tone, at 84 decibels, or an automobile horn sounded near the subject in a quiet room) will cause depression of both rhythms after a latency of from 0.1 to 0.2 second; the precentral beta potentials, however, will return after from one to two seconds, while the occipital alpha potentials may be blocked for from fifteen to twenty seconds (fig. 2 *B* and *C*). Likewise, with a strong light stimulus in a dark room the beta potentials may be affected for about one second, while the occipital alpha potentials may remain blocked much longer.

However, the beta potentials may be blocked independently of any appreciable effect on the occipital alpha waves with moderate intensities of tactual or auditory stimulation (fig. 3). Unexpected tactual stimuli seem to be the most suitable for differential blocking of the precentral beta potentials (fig. 4). This is in accord with our assumption that these potentials are referable to the sensorimotor areas [9]

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9. The close functional association of the postcentral and the precentral area in the monkey, as shown by Dusser de Barenne [17b] from changes in sensitivity following the local application of strychnine, and the close similarities we have found (Rheinberger, Margaret B., and Jasper, H. H.: *Am. J. Physiol.* **119**:186-196 [June] 1937) between the electro-encephalograms for these two regions recorded directly from the cortex in the cat have led us to speak of the sensorimotor cortex as a functional unit in this connection. Also, our methods of localization from the surface of the head in man are not sufficiently refined to assure distinction between the precentral and the postcentral region. Measurements for electrode placements in our experiments were designed to place the pair of electrodes over the precentral region, so that we have spoken of the records from leads so placed as precentral records; certainly, in some cases the electrodes may be more nearly over the postcentral region. We know only that they are placed over the general region of the central fissure and are more often precentral than postcentral.

in the region of the central fissure and that they are of local functional importance (rather than representative only of metabolic processes) for this region, somewhat as are the occipital alpha waves for the occipital region.

Berger pointed out that light stimuli which block the alpha rhythm seem to have no effect on the beta rhythm. We have repeatedly observed this selective blocking of the alpha potentials with visual stimulation of moderate intensity (fig. 3*A*). This serves to demonstrate the functional independence of the two rhythms under stimulating situations which permit a more highly differentiated response of one cortical region as opposed to those which produce a generalized "mass" response of the entire cortex.

11. Relation to Adjacent Muscle Potentials: We have presented evidence in a previous report [5] which demonstrates that the precentral beta potential is not altered by contraction of the muscles of the head near the pair of electrodes over the precentral region, except for the introduction of muscle spikes in the record. Moreover, the record of muscle potentials recorded directly over these muscles does not resemble that of precentral beta potentials obtained simultaneously from a pair of electrodes over the precentral region, near the median line.

COMMENT

We have included in the present report our results on the normal autonomous bio-electric activity of the occipital and precentral regions of the human cortex as recorded through the unopened skull, in order to demonstrate in some detail the type of differentiation that is possible between these two regions. We have shown in a previous report [5] that the limits of regional differentiation from the surface of the head are much easier to determine in pathologic conditions with marked localized disturbances in cortical activity or in cases in which there is gross disturbance in the normal amount of synchronized activity between different areas. The continuation of such studies in both normal and pathologic conditions has shown that regional differentiation between each of the five regions of the head is possible if relative amplitudes for the more proximate regions are given adequate consideration. Each of these five regions (frontal, precentral, parietal, occipital and temporal) gives sufficiently characteristic records in the normal conscious subject that one can usually identify the region from the record alone, without reference to the protocols except for a few marked individual differences, which are difficult to explain. In most cases this differentiation is obvious only with the standard paired leads, the records from different regions being much more alike with diffuse monopolar leads. The first method of localized recording is proving particularly valuable in our studies of various pathologic conditions of the cerebral cortex.

Origin of Alpha Potentials.—In regard to the argument of Adrian and Yamagiwa that Berger's alpha rhythm is entirely of occipital origin, as proved by its peculiar sensitivity to vision, we have corroborated

Berger's original conclusion (as have Gibbs, Davis and Lennox [10] and Loomis, Harvey and Hobart [11]), namely, that the alpha rhythm is readily blocked by nonvisual stimuli. In a recent article [12] it was pointed out that the important quality of a stimulus of any kind which determines its effectiveness on the alpha rhythm is that it possess a definite "signal value" or "arousal value" for the subject; it was also suggested that the similarity between these stimulating situations and those which produce a pupillary response seems to link the alpha rhythm with the autonomic system more closely than with the visual system as such. Of course, if one considers the amount of "mass action" or the interrelationship between areas involved in the response of any given region of the brain, the alpha potentials might still be purely of occipital origin and be affected by nonvisual stimuli.

Berger [1a] and Loomis, Harvey and Hobart [8] observed the alpha rhythm in congenitally blind persons and showed that it may be blocked readily by auditory stimuli. The prepotency of visual stimuli in normal human subjects may indicate the prepotency of such stimuli for the total orientation of the organism ("attention"), so that in the blind auditory stimuli may well assume the rôle of visual in this regard.

Though the 10 cycle alpha rhythm is most regular and of greatest amplitude over the occipital region of the head in most normal conscious subjects, subjects were observed in whom the occipital alpha rhythm was less prominent than rhythmic potentials from other regions. All subjects showed synchronous activity sufficient to be detected from the surface of the head in regions other than the occipital. That the same frequency may be observed simultaneously from widely separated cortical fields, when precautions are taken to obtain electrically independent records from these fields, probably indicates a subcortical pacemaker rather than a single cortical source for activity of this frequency. Kornmüller [13] reported that one finds a great deal of synchronism in the spontaneous rhythms of the rabbit's cortex, even from widely separated areas (with electrodes placed directly on the cortex), so that a physiologic rather than an electrical explanation of such synchronism in man is not improbable.

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10. Gibbs, F. A.; Davis, H., and Lennox, W. G.: The Electro-Encephalogram in Epilepsy and in Conditions of Impaired Consciousness, Arch. Neurol. & Psychiat. **34**:1133-1148 (Dec.) 1935.

11. Loomis, A. L.; Harvey, E. N., and Hobart, G.: Electrical Potentials of the Human Brain, J. Exper. Psychol. **19**:249-279, 1936.

12. Jasper, H. H., and Cruikshank, R. M.: Electro-Encephalography: II. Visual Stimulation and the After-Image as Affecting the Occipital Alpha Rhythm, J. Gen. Psychol. **17**:29-48, 1937.

13. Kornmüller, A. E.: Die bioelektrischen Erscheinungen architektonischer Felder des Grosshirnrinde, Biol. Rev. **10**:383-426, 1935.

Comparison with Cyto-Architectonic Differentiation in Animals.—Kornmüller [14] reported that the various cyto-architectonic cortical areas may be differentiated almost as well by their autonomous bio-electric activity as by their cell structure. He reported such differentiation for the rabbit and monkey from records taken directly from the surface of the dura or the cortex. The characteristic bio-electric activity of the area striata in the rabbit is represented by slow, smooth waves, at about 3 per second, as compared with that of the area precentralis agranularis, where the predominant rhythm is from about 10 to 12 per second. Kornmüller concluded that the predominance of slow waves may be related to that of granular cells and the greater proportion of the more rapid waves to the agranular type of cyto-architectonic structure. This is an interesting correlation, and one which should apply to the bio-electric activity of the human cortex as well as to that of the rabbit, since the cyto-architectonic structure of the two cortices are not greatly different. The differentiation we have obtained in our studies by limiting the region of the head from which potentials are recorded indicates that the differentiation of the precentral and the occipital region in man may be nearly as distinct (although, naturally, not nearly as well localized from the surface of the head) as it is in the rabbit. Furthermore, the predominance of the beta potentials in the precentral region, at about 25 per second, in contrast to that of the alpha potentials in the occipital region, at about 10 per second, is comparable to the relative differentiation between these two regions that was reported by Kornmüller for the rabbit.

Our experiments tend to corroborate the work of Kornmüller on animals, except for the marked individual differences we observed in human material and for important changes in the cortical potentials from a given region of the brain, depending on the conditions of the experiment (some of which are, as yet, ill defined). This marked variability in a given region of the brain has also been observed in the cat in studies performed in collaboration with Dr. Margaret Rheinberger.[15] We have concluded from these studies that, since wide variations in the characteristics of the bio-electric activity of a given region occur with variations in the local and general excitatory conditions of the tissue, regional differentiation may be due to differential excitatory conditions existing between regions, as well as to the cell structure itself. The electrical activity of the cortex differs in frequency, magnitude, form and regularity, depending on the excitatory condition,[15] metabolic activ-

14. Kornmüller, A. E.: Bioelektrische Erscheinungen architektonischer Felder, Deutsche Ztschr. f. Nervenh. **130**:44-60, 1933.

15. Jasper, H. H.: Cortical Excitatory State and Synchronism in the Control of Bioelectric Autonomous Rhythms, in Symposium on Quantitative Biology, Cold Spring Harbor, L. I., N. Y., The Biological Laboratory, 1936.

ity [16] and structure (both regional [14] and laminar [17]) of the cortical areas contributing to the complex of potentials obtained.[18]

Local "On" and "Off" Effects.—We have omitted from discussion in this report the localized potential waves which occur as a result of afferent stimulation and which appear to be distinct from the autonomous rhythm in a given region. These are the *Feldaktionsströme* of Kornmüller, as opposed to the *Feldeigenströme*. Examples of these slow waves from the precentral region of the head following tactual stimulation are shown in figure 5 *A*, *C* and *D*. With the proper electrode placements, they may also be recorded regularly from the surface of the head over the occipital region in response to a visual stimulus of moderate intensity.[19] These "on" and "off" effects in central nerve tissue have been reported by many authors from records taken directly from the cortex. They provide an additional means of localizing cortical function, but are limited in man by the fact that they originate in the primary sensory projection areas, which are not readily accessible to the surface of the head in most cases, and by the fact that they are often masked by spontaneous rhythms.

SUMMARY AND CONCLUSIONS

A method has been described which makes possible localized recording of the bio-electric potentials of the normal human cortex through the unopened skull. A detailed comparison of the records thus obtained from the occipital and the precentral region has been presented. It is concluded that:

1. The autonomous bio-electric activity from each cortical region is complex. Two regions have been studied by us—the occipital and the precentral. Each has a different characteristic activity. There are alpha components, at frequencies of from 8 to 13 per second, beta components, at frequencies of from 17 to 30 per second, and possibly gamma com-

16. Hoagland, H.: Temperature Characteristics of the "Berger Rhythm" in Man, Science **83**:84-85 (Jan. 24) 1936. Jasper.[15]

17. (*a*) Dusser de Barenne, J. G., and McCulloch, W. S.: Some Effects of Laminar Thermocoagulation upon the Local Action Potentials of the Cerebral Cortex of the Monkey, Am. J. Physiol. **114**:692-694, 1936. (*b*) Dusser de Barenne, J. G.: Experimental Researches on Sensory Localization in the Cerebral Cortex of the Monkey (Macacus), Proc. Roy. Soc., London, s.B **96**:272-291, 1924; Experimentelle Untersuchungen über die Lokalisation der sensiblen Funktionen in der Grosshirnrinde beim Affen (Macacus), Zentralbl. f. d. ges. Neurol. u. Psychiat. **38**:273, 1924; Experimentelle Untersuchungen über die Lokalisation des sensiblen Rindengebietes im Grosshirn des Affen (Macacus), Deutsche Ztschr. f. Nervenh. **83**:273-299, 1924-1925.

18. Jasper, H. H.: Cortical Excitatory State and Variability in Human Brain Rhythms, Science **83**:259-260 (March 13) 1936.

19. Jasper, footnotes 15 and 18.

ponents, of still higher frequencies (from 35 to 48 per second), which are usually obscured by the more prominent alpha and beta potentials.

2. The occipital alpha potentials are distinct in cortical origin from the precentral alpha potentials, as shown by the differential reaction to stimulation under certain conditions and by their spontaneous appearance in one region independent of that in the other, even though they are usually (though not always) of the same frequency in both regions, usually occur with constant phase relations and are ordinarily affected by the same afferent stimulation.

3. The characteristic electro-encephalogram of the precentral region is composed of a greater proportion of beta potentials than is that of the occipital region.

4. The precentral beta potentials occur at an average frequency of about 25 per second and are independent of the occipital alpha potentials in frequency, regularity and response to afferent stimulation. Since they are most readily depressed by tactual stimulation and are not usually affected by stimulation with light (the reverse being true for the occipital alpha potentials), it is thought that they represent functional activity of the sensorimotor region analogous to the activity of the occipital region represented by the occipital alpha potentials.

5. Both the occipital alpha and the precentral beta rhythm may be increased or decreased in frequency by the same general excitatory conditions (excitement, drowsiness and sleep) and by the same general metabolic conditions (as shown by their variations with body temperature).

6. Localized "on" effects are recorded in the precentral region after reflex tactual stimulation and in the occipital region after visual stimulation.

Dr. Margaret Rheinberger gave assistance in reading records and correcting the manuscript.

FRIEDREICH'S ATAXIA

A HISTOPATHOLOGIC STUDY

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After Friedreich (1863 [1]) described the form of ataxia which bears his name, the clinical and pathologic features of the morbid condition which he established were the subject of much controversy. Thus, Friedreich and Schultze [2] considered it a disease of the spinal cord (combined degeneration), while Senator,[3] on purely clinical grounds, looked on it as a disease of the cerebellum. Marie in 1893,[4] in a review of the cases published under the head of Friedreich's disease, placed some in a separate group, which he designated as heredocerebellar ataxia. In 1900 Dejerine and Thomas [5] described olivopontocerebellar atrophy, and in 1909 Léjonne and Lhermitte [6] reported a case of so-called olivorubrocerebellar atrophy. The clinical features in the case of Dejerine and Thomas resembled those of both Friedreich's disease and Marie's heredocerebellar ataxia, while in the case described by Léjonne and Lhermitte the clinical picture was mainly that of Weber's syndrome. Pathologically, the condition was globar atrophy of the cerebellum combined with degeneration of the medullary olives and the superior

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From the Division of Neuropathology, the University of Illinois College of Medicine.

Read by title at the Sixty-Third Annual Meeting of the American Neurological Association, June 5, 1937, Atlantic City, N. J.

1. Friedreich, N.: Ueber degenerative Atrophie der spinalen Hinterstränge, Virchows Arch. f. path. Anat. **26**:391 and 433, 1863; **27**:1, 1863.

2. Schultze, F.: Ueber die Friedreich'sche Krankheit und ähnliche Krankheitsformen, nebst Bemerkungen über nystagmusartige Zuckungen bei Gesunden, Deutsche Ztschr. f. Nervenh. **5**:27, 1894; Erwiderungen auf den zweiten Artikel von Senator über hereditäre Ataxie, Berl. klin. Wchnschr. **31**:760, 1894.

3. Senator, H.: Ueber hereditäre Ataxie (Friedreich'sche Krankheit), Berl. klin. Wchnschr. **30**:489, 1893.

4. Marie, P.: Sur l'hérédo-ataxie cérébelleuse, Semaine méd. **13**:444, 1893.

5. Dejerine, J., and Thomas, A.: L'atrophie olivo-ponto-cérébelleuse, Nouv. iconog. de la Salpêtrière **13**:330, 1900.

6. Léjonne, P., and Lhermitte, J.: Atrophie olivo-rubro-cérébelleuse: Essai de classification des atrophies du cervelet, Nouv. iconog. de la Salpêtrière **22**:605, 1909.

cerebellar peduncles. The case of Léjonne and Lhermitte is unique and so far has not been duplicated in the literature. For this reason, this form of atrophy may be disregarded for the moment; only Friedreich's disease, Marie's heredocerebellar ataxia and olivopontocerebellar atrophy should be considered in the presence of a clinical picture in which the dominant features are certain disturbances of gait, speech and reflexes and occasional nystagmus. The clinical similarity in the three aforementioned forms may be so great that a differential diagnosis is sometimes difficult to make. For instance, the main differential characteristics of olivopontocerebellar atrophy, as emphasized by Dejerine and Thomas, are late onset and a hereditary factor. However, Friedreich's, and especially Marie's, ataxia may start also late in life, while olivopontocerebellar atrophy may be hereditary. Furthermore, it was possible to prove that the underlying pathologic features of what Marie designated as heredocerebellar ataxia are those of olivopontocerebellar atrophy—that these two conditions are one disease process.[7] The three morbid entities should thus be reduced to two: Friedreich's disease and Marie's heredocerebellar ataxia (olivopontocerebellar atrophy). Even these two morbid conditions are looked on by some not as distinct entities but as one disease process—heredo-ataxia, with Friedreich's disease as its cerebellospinal type and Marie's ataxia as its cerebellar form.[2] If this is the case, Marie's ataxia (or olivopontocerebellar atrophy) should possess pathologic features which are seen in Friedreich's disease and vice versa. A study of this problem on the basis of two cases and a review of the literature, leads me to the conclusion that Friedreich's and Marie's ataxia are different morbid entities.

REPORT OF CASES

CASE 1.—A man aged 27 had been well until the age of 10 (except for the usual diseases of childhood), when he began to exhibit awkward movements. The gait became "staggering," and there was a tendency to fall, usually to the right. The disorder in gait progressed, and at the age of 17 neither walking nor standing was possible because of the development of a deformity of the feet. At the age of 19 pains were experienced in the shoulders, arms and legs, and the temperature was often elevated (probably because of frequent attacks of sore throat). One week prior to entrance to the hospital the patient became subject to cramplike pains in the abdomen and attacks of vomiting after meals. During these attacks he became "delirious;" the face turned greenish yellow; saliva drooled from the mouth, and there was shortness of breath. Two years before his admission the patient had a "stroke" in which his mouth was "drawn up to the right side" and saliva drooled. Recovery followed within one month. For the last seventeen years there were disturbances in speech, nystagmus "to the right," sluggish patellar reflexes, Oppenheim and Babinski signs bilaterally, flat feet and oxycephalia. The

7. Hassin, George B., and Harris, Titus: Olivopontocerebellar Atrophy, Arch. Neurol. & Psychiat. **35**:43 (Jan.) 1936.

mental condition was always "exceptionally good." The spinal fluid was clear and "under slightly increased pressure" and contained 10 cells per cubic millimeter. Death followed the appearance of bronchopneumonia.

CASE 2.—The brain and spinal cord in this case were given to me by Dr. M. R. Broman, of the Swedish Covenant Hospital of Chicago.

A tanner, aged 67 at the time of death, had been an inmate of an old people's home. As he was not at any time a patient in the hospital, no clinical record was available.

PATHOLOGIC OBSERVATIONS

As the pathologic features in the two cases were alike, they will be described together.

The spinal cord in each case was greatly reduced in size, and the pia-arachnoid was thickened. The medulla, pons and cerebellum exhibited in general no gross changes, although the cerebellum in case 1 was somewhat small. Sections of the spinal cord stained by the Pal-Kultschitzky method showed changes that are considered to be typical of Friedreich's disease (figs. 1 and 2). The cervical, thoracic, lumbar and sacral regions exhibited marked degeneration of the posterior columns, especially of the tract of Goll, and of the lateral columns (pyramidal and direct cerebellar tracts), with preservation at some levels (the sacral, especially) of the cornucommissural and the entrance zone (cervical region) in the posterior columns and of the lateral limiting zone in the lateral columns. The posterior roots, as well as Clarke's columns, in which the fibers and ganglion cells were reduced in number, were degenerated at some levels (dorsolumbar) (*P.r.*, fig. 2). The anterolateral columns were not involved.

Additional studies with nuclear, silver and glial staining methods revealed glial scarring (fig. 4) in areas which appeared colorless in sections stained by the Pal-Kultschitzky method. Such areas, however, occasionally contained a few well preserved axons (fig. 4) which were deprived of myelin. Areas less completely destroyed exhibited numerous nerve fibers in the early stages of degeneration: swelling of the myelin, excessive numbers of Elzholz' bodies (*Ax* in figure 4) and slight proliferation of the glia cells with the formation of myelophages. The glial scar was represented by wavy glia fibrils (fig. 4), which formed dense bundles, ran a parallel course and contained numerous glia nuclei but hardly any cytoplasmic astrocytes and no gitter cells. The fibrils were thin and long, did not cross each other and resembled slightly the whorls (*tourbillons*) of Dejerine. The glia fibrils replaced the destroyed nerve fibers, the course of which they followed, giving a picture of isomorphous gliosis. The same condition obtained in the lateral columns and, what is even more noteworthy, in the apparently well preserved anterior columns. Figure 5 shows such degenerated nerve fibers—a myelophage in the form of a glial ring enveloping a fragment of myelin (*M*), the so-called Marchi globules (*B*) of a broken-up nerve fiber and swollen myelin (*A*) with a thickened axis-cylinder. Such changes represent an early stage of nerve degeneration, in contrast to the advanced degenerative changes in the posterior columns. These were especially marked in the column of Goll and decreased successively in degree of severity in the column of Burdach, the crossed pyramidal tract (fig. 6), the direct and crossed spinocerebellar tracts and the anterior pyramids. In short, the entire white parenchyma of the spinal cord was more or less affected. The columns of Clarke exhibited severe destruction of the ganglion cells and their nerve fibers, while the ganglion cells of the anterior and posterior

horns showed no striking microscopic or reactive glial changes (in specimens stained with toluidine blue or by the method of Bielschowsky). The meninges and the blood vessels, however, were moderately hyperplastic and had no inclusions in the Virchow-Robin adventitial spaces (fig. 6). The anterior roots (upper portion, fig. 3) exhibited no changes, while the posterior roots (lower portion, fig. 3) usually appeared altered, depending, however, on the area of the cord

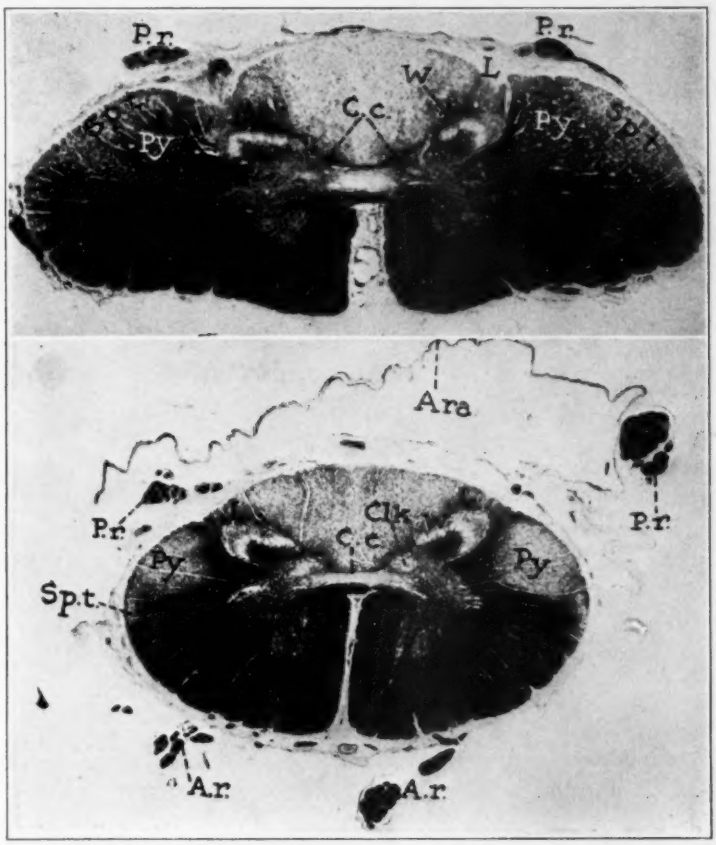

Fig. 1.—Above is a section of the seventh cervical segment. The posterior root (*P.r.*), Lissauer's zone (*L*) and small parts of Westphal's radicular (*W*) and the cornucomissural (*C.c.*) zone are preserved on both sides. The posterior columns, especially the column of Goll, and the dorsal spinocerebellar tracts (*Sp.t.*) are markedly degenerated; the crossed pyramidal tracts (*Py.*) are only slightly involved, while the anterior and the rest of the lateral columns appear normal.

Below is a section of the twelfth thoracic segment. *Ara* represents the arachnoid membrane; *A.r.*, the anterior roots, which, like the posterior (*P.r.*), are normal, and *Clk*, Clarke's columns, which are degenerated. Lissauer's zone is normal, as in the cervical segment; the pyramids (*Py*) and the posterior spinocerebellar tracts are degenerated, and the cornucommissural zone (*C.c.*) is partially preserved. Pal-Kultschitzky stain.

affected. As figure 1 shows, the posterior roots (*P.r.*) appeared practically normal in the cervical and thoracic areas but were affected in the lumbosacral region (*P.r.*, fig. 2), especially in the cauda equina. Some, a very few, nerve fibers of the posterior roots exhibited well preserved myelin and axons (lower portion, fig. 3),

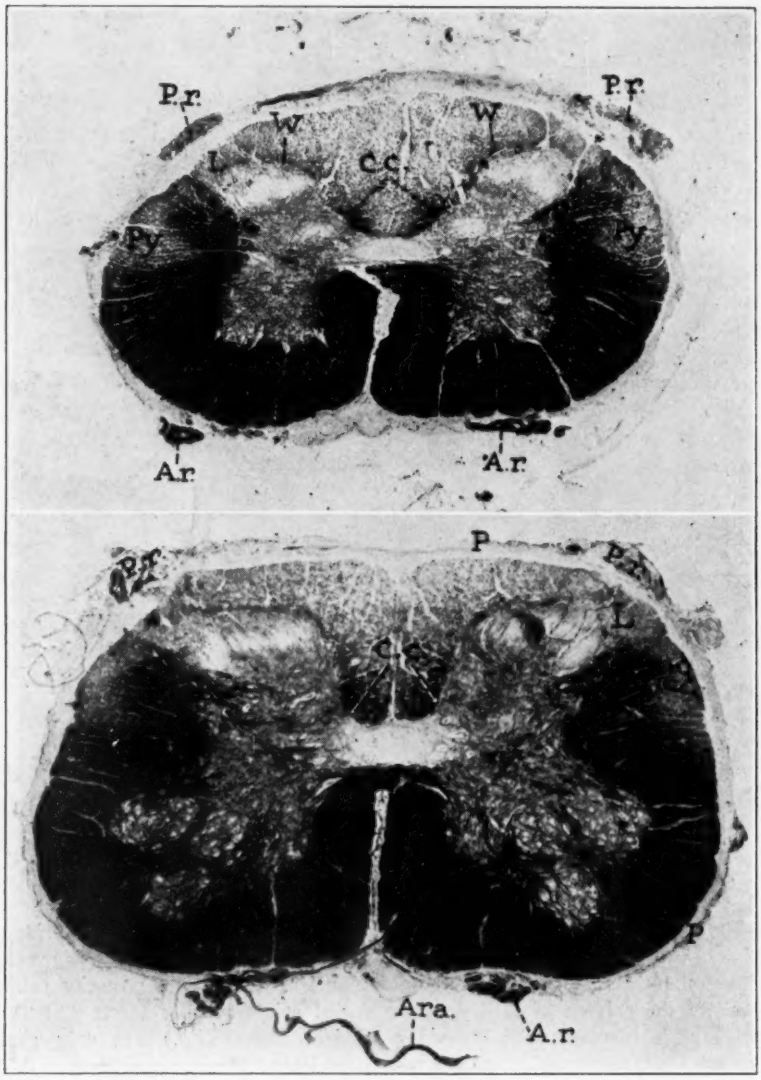

Fig. 2.—Sections of the second lumbar segment (above) and of the first sacral (below). The posterior roots (*P.r.*) are degenerated; the anterior roots (*A.r.*) are normal; Lissauer's zone (*L*) appears paler than in the cervicodorsal segments and is only slightly affected; Westphal's entrance root zone (*W*) is more involved, but the cornucommissural zone (*C.c.*) is better preserved, especially in the sacral region, than in the cervicodorsal segments. Pal-Kultschitzky stain.

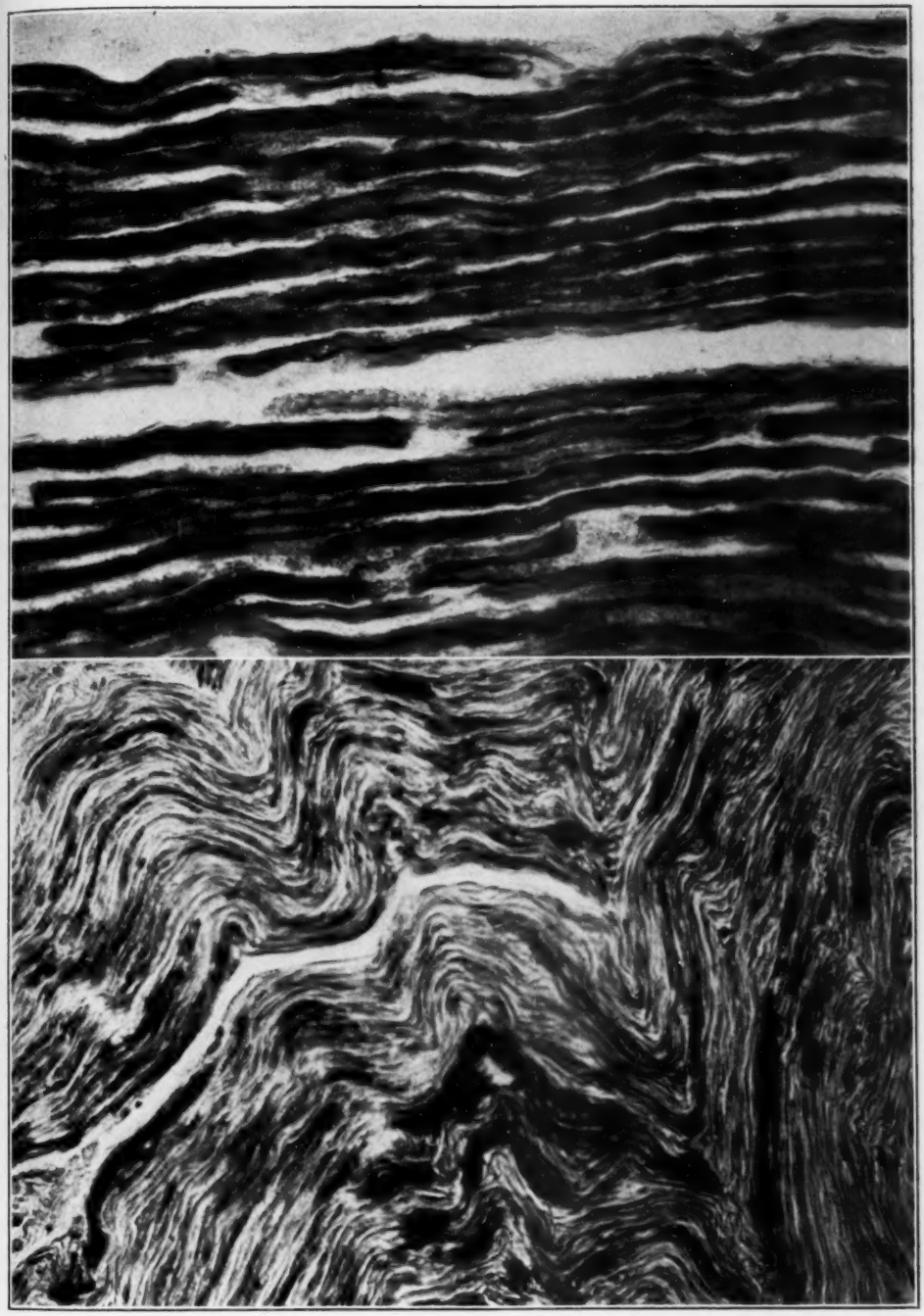

Fig. 3.—Sections of an anterior root (above) and a posterior root (below) taken from the same level of the cauda equina. The description is given in the text. Van Gieson stain.

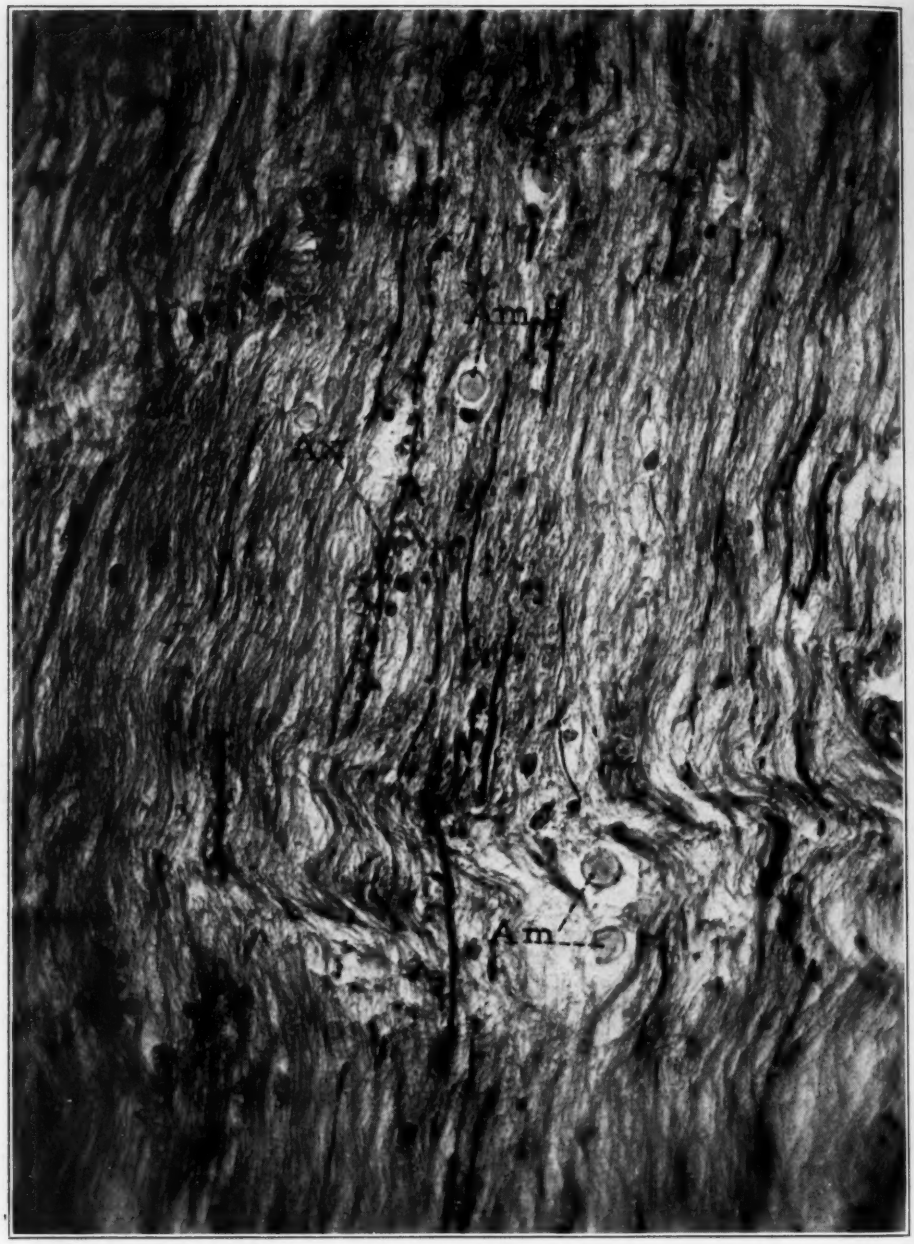

Fig. 4.—Longitudinal section of the column of Goll. The black lines are axons, along some of which (*Ax*) are broken myelin drops in the form of Elzholz' bodies; the round, homogeneous formations are amyloid bodies (*Am*); the rest of the tissue (especially in the lower half of the picture on the right) is represented by bundles of dense fibrillary glia (glial scar), with few nuclei. Bielschowsky stain.

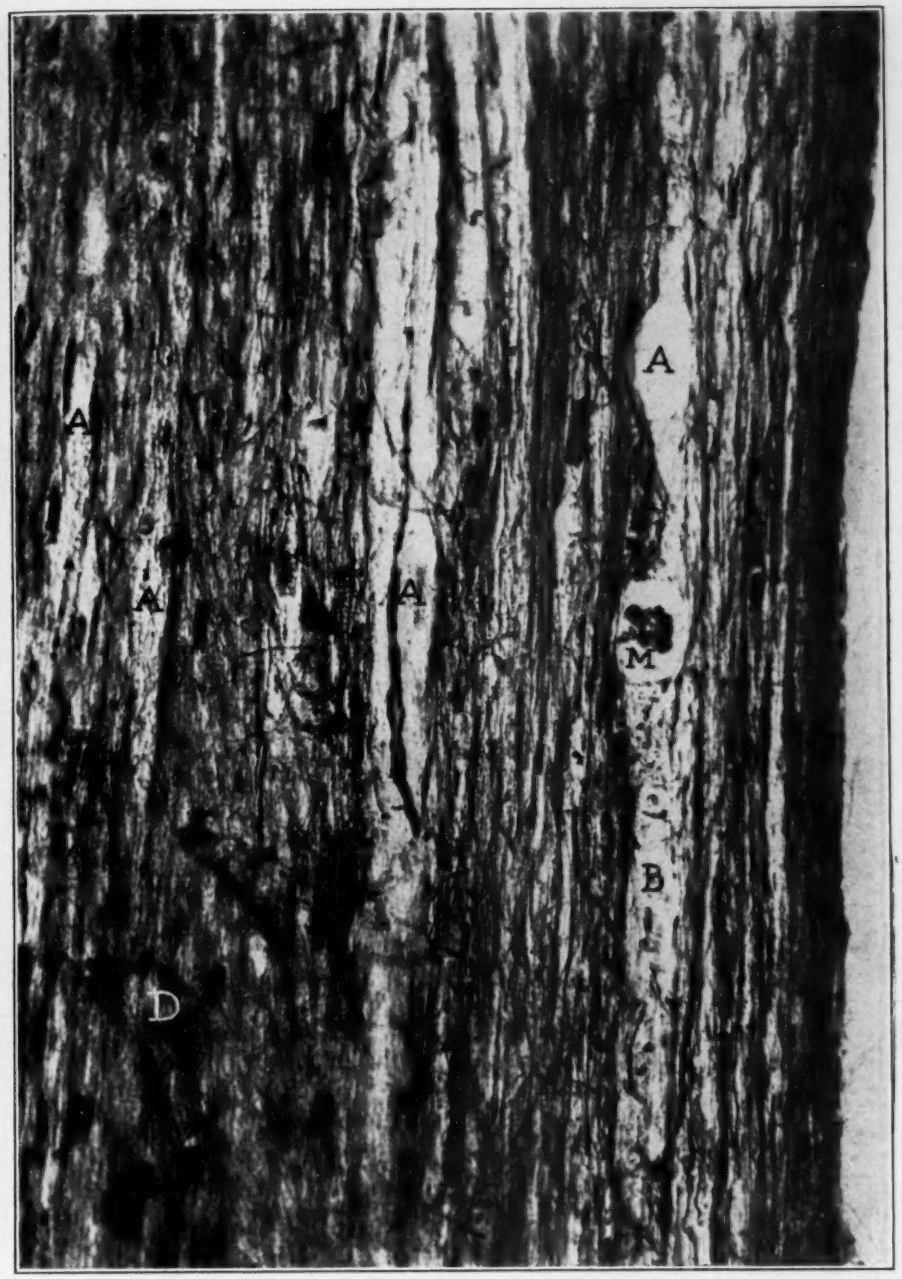

Fig. 5.—Longitudinal section of the anterior column which in figures 1 and 2 appeared normal with the Pal-Kultschitzky stain. Among the rows of normal axons are several pathologic nerve fibers. At *A* the myelin is swollen, as well as the axon (in the center of the picture, at *A*); at *B* the myelin is represented by a row of Marchi globules; at *M* a fragment of myelin is enclosed within a myelophage, and at *D* the gray matter of the spinal cord is shown. Bielschowsky stain.

but the majority of the root fibers were destroyed and replaced by bundles of dense connective tissue and immensely proliferated endoneurial cells. The course and distribution of the latter were similar to those described in secondary degeneration of peripheral nerves and illustrated in figure 10 of my contribution on this subject.[8] They were also similar to the degenerated bundles pictured in the lower half, at the right, of figure 4 of the present paper.

The medulla, pons, cerebellum and cerebrum were studied carefully, especially in sections stained by the method of Bielschowsky, but nothing pathologic was observed. This was true also of the cerebellum, in which the ganglion cells, the

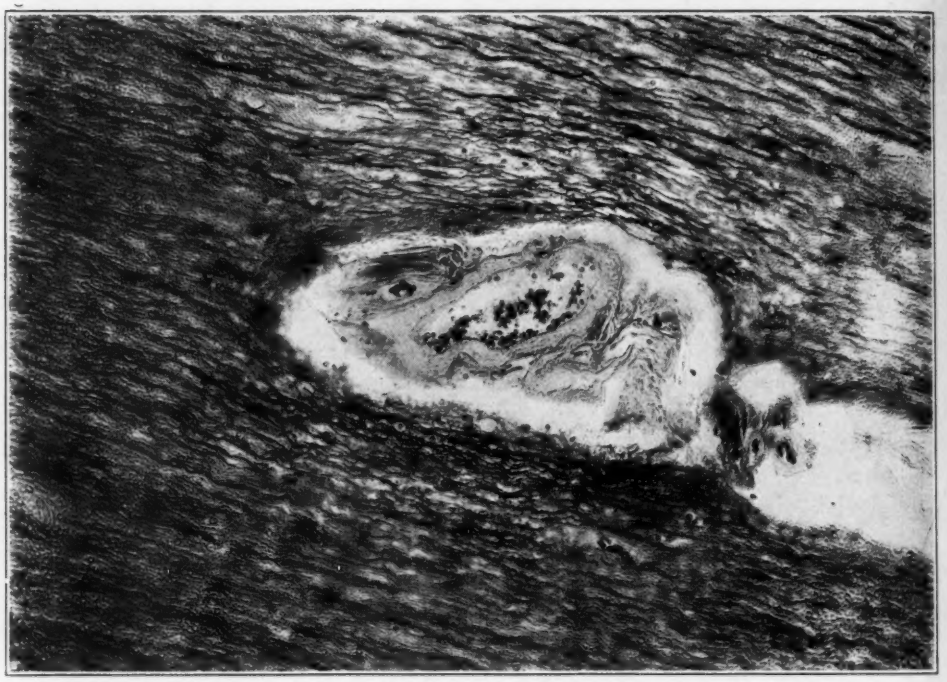

Fig. 6.—This section represents a better preserved portion of the spinal cord (the pyramidal fibers of the cervical region, shown in figure 1). In the right half of the figure is a glial scar in the form of isomorphous gliosis. The center of the picture is occupied by patent blood vessels, the walls of which are hyperplastic, but not infiltrated. Bielschowsky stain.

glia, the afferent and efferent nerve fibers of the white substance of the granular and molecular layers (mossy, climbing and basket fibers) and of the white substance of the cerebellum and the blood vessels showed no changes (fig. 7). Only one spinal ganglion was available for proper histologic examination; it showed no particular changes.

8. Hassin, George B.: Peripheral Nerves: Anatomic and Pathologic Considerations, Arch. Neurol. & Psychiat. **27**:58 (Jan.) 1932.

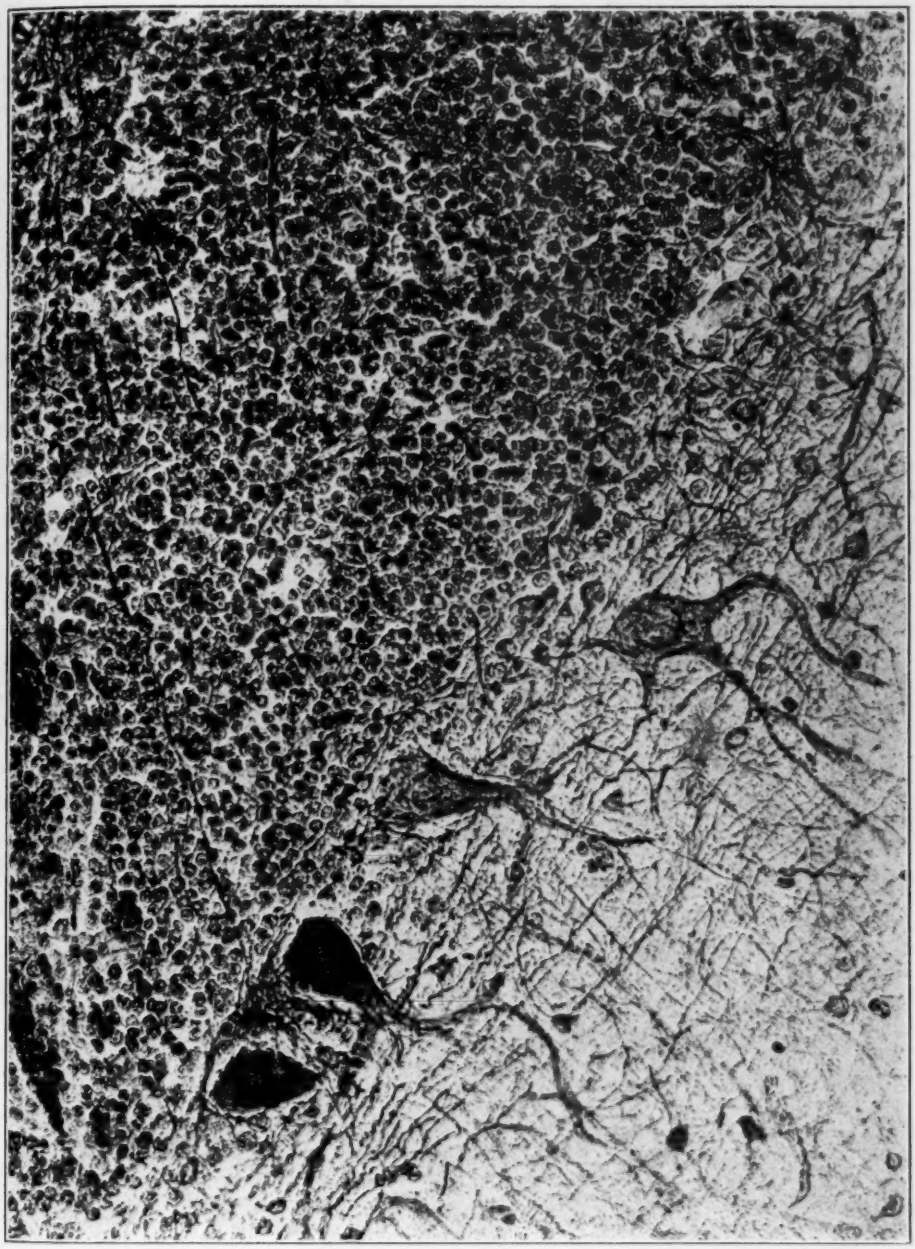

Fig. 7.—This section represents Purkinje cells and their dendrites, climbing and basket fibers and the granular layer with mossy fibers (black lines) crossing them, all of which are normal. Bielschowsky stain.

SUMMARY AND COMMENT

Changes were observed only in the spinal cord. They may be designated as combined degeneration of the posterior and lateral columns; marked involvement of Clarke's columns and of the posterior roots (with preservation of the anterior roots); mild hyperplasia of the meninges and walls of the blood vessels, and absence of signs of inflammation. The pathologic features were similar to those observed in any other degenerative condition, such as tabes, multiple sclerosis, subacute combined degeneration of the cord and caisson disease. The changes were not inflammatory, as was claimed by Friedreich,[1] Blocq and Marinesco[9] and others; nor were they secondary to primary glial proliferation, as was stated by Dejerine and Letulle.[10]

The type of sclerosis which replaced the nerve fibers in the affected columns was everywhere that which Dejerine called "pure;" that is, it consisted of glial fibers. No "mesodermal" or "vascular" sclerosis was present in the lateral columns, as was claimed by Dejerine and his co-workers. The whorls (*tourbillons*), which Dejerine stated were typical of Friedreich's disease, are manifestations of isomorphous sclerosis and are rare in the form described by him. Schultze never saw them, nor were they typical in my cases. After Dejerine, only Mingazzini and Perusini[11] pictured them clearly. In my cases the degeneration was far advanced, which was natural, for the illness in both instances lasted several decades. Yet, even in the cords in these cases one could find signs of beginning nerve degeneration, which evidently starts early, continues and stops only with death. The concomitant reaction of the glia, with the formation of myelophages, is so similar to what is observed in secondary degeneration of the spinal cord following an experimental or accidental injury of the brain that a detailed discussion is superfluous. It suffices to state that in a cerebral injury (to the motor area, for instance) the parts of the nerve fibers which are directly affected are the first to degenerate. The peripheral, healthy stump of the injured nerve fiber ultimately perishes also, causing a concomitant, secondary reaction of the glia. Consideration of the glial changes as primary is groundless, for the glia does not form continuous tracts as do nerve fibers and its injury and reactions are always local. This is

9. Blocq, P., and Marinesco, G.: Sur l'anatomie pathologique de la maladie de Friedreich, Semaine méd. **10**:76, 1890.

10. Dejerine, J., and Letulle, M.: Sur la nature de la sclérose des cordons postérieurs dans la maladie de Friedreich (sclérose nevroglique pure), Semaine méd. **10**:81, 1890. Dejerine, J.: Note sur l'anatomie pathologique de la maladie de Friedreich, Compt. rend. Soc. de biol. **2**:479, 1890.

11. Mingazzini, G., and Perusini, G.: Two Cases of Familial Heredospinal Atrophy (Friedreich's Type) with One Autopsy, and One Case of So-Called Abortive Form of Friedreich's Disease, J. Ment. Path. **6**:14, 57 and 104, 1904-1905.

also true of other degenerative states, such as sclerotic atrophy of the cerebellum, multiple sclerosis, subacute combined degeneration of the cord and peripheral nerve injuries, in which the parenchymatous changes are primary and those of the glia secondary.

In their evolution the changes resemble entirely those existing in experimental secondary degeneration; they should consequently be considered in the same light; that is, the parenchyma is involved first and the glia afterward. The hereditary features of Friedreich's disease also speak for the degeneration's being primarily parenchymatous, for hereditary degeneration of the glia is so far unknown, either clinically or pathologically. The hereditary factor would also eliminate inflammation or a vascular factor as the essence of this disease, for an inflammatory process is never hereditary. It is noteworthy that Schultze, the pioneer student of the pathology of Friedreich's disease, designated the disease as combined degeneration of the cord. In its gross features it certainly resembles the subacute form of the latter, and without knowledge of the clinical history in a given case a differential pathologic diagnosis of Friedreich's disease and subacute combined degeneration of the cord is not possible. There are differences, however. For instance, the cribriform appearance so common in subacute combined degeneration of the cord is not in evidence in the spinal cord in Friedreich's ataxia because of the time element; nor is the fibrous glia, which is typical of Friedreich's disease, a common feature in subacute combined degeneration of the cord. However, it occurs when the duration of the process is protracted, as in a case reported by Stone and me.[12] The topographic distribution of the degenerative changes and their general microscopic characteristics justify classification of the pathologic features of Friedreich's disease as those of subacute combined degeneration. The word "subacute" should, of course, be replaced by "chronic" because of the protracted course. It is probable that in many cases of subacute combined degeneration of the cord, in which the patients have been treated with liver and kept alive for many years, changes may be exhibited in the cord which are similar to those of Friedreich's ataxia.

The changes in the columns of Clarke, which are marked in Friedreich's disease, are secondary to the long-standing, retrograde degeneration of the dorsal spinocerebellar tracts which originate in them and in which they cause the so-called axonal reaction. Features of this reaction can be seen even under normal conditions in the ganglion cells of Clarke's column.

The changes outlined make up the pathologic features of pure, uncomplicated Friedreich's disease. As this morbid condition may be

12. Hassin, George B., and Stone, T. T.: Subacute Combined Degeneration of the Spinal Cord, Arch. Neurol. & Psychiat. **34**:401 (Aug.) 1935.

complicated by such anomalies as atrophy of the optic nerve, retinitis pigmentosa, spina bifida and atrophy of the small muscles of the hands, the pathologic features may accordingly become more complex and show changes in the ganglion cells of the spinal cord or cortex. In cases of the pure, uncomplicated type that were studied impartially there were exhibited no changes that are observable in Marie's form, in which the medulla, pons and cerebellum are affected. In a richly illustrated monograph from Cajal's laboratory, Estable [13] endeavored to prove that in Friedreich's ataxia there are diffuse changes in the ganglion cells (Purkinje, basket and Golgi cells) of the cerebellum, which he termed "hypocytomorphosis." The neurofibrils are shrunken, causing atrophy of the ganglion cells, or are fragmented, producing regressive changes in the dendrites; the axons exhibit retraction balls and are hypertrophied, and the mossy and climbing fibers are reduced in number because of retrograde degeneration. The dentate nucleus was observed to be intact. Estable did not mention any changes in the glia. The parenchymatous changes which he studied with one of Cajal's silver staining methods were by no means as striking as those seen in the spinal cord. They probably were like the cerebellar changes described by Mott,[14] Spiller [15] and Winkelman and Eckel [16]—accidental or secondary to those in the spinal cord. No changes in the cerebellum were present in my cases or in those reported by Friedreich and Schultze, Burr,[17] Rütimeyer,[18] Dejerine and Letulle,[10] Mingazzini and Perusini,[11] Bonnus [19] and others, though sclerosis or diminution in the size of the cerebellum was occasionally mentioned (Schultze, Winkelman and Eckel and Burr).

In contrasting such rare extraspinal changes in isolated cases of Friedreich's disease with what is seen in Marie's ataxia, one is struck by the extensive involvement in the latter of the medulla, pons and cerebellum. In cases of long standing, the changes may be combined

13. Estable, Clemente: Zur Histopathologie der Friedreich'schen Krankheit nebst einigen Bemerkungen über die Leitungsbahnen des Rückenmarkes, Trav. du lab. de recherches biol. de l'Univ. de Madrid **27**:1, 1931.

14. Mott, Fred: Case of Friedreich's Disease with Autopsy and Systematic Microscopic Examination of the Nervous System, Arch. Neurol. Path. Lab. London County Asyl. **3**:180, 1907.

15. Spiller, W. G.: Friedreich's Ataxia, J. Nerv. & Ment. Dis. **37**:411, 1910.

16. Winkelman, N. W., and Eckel, J. L.: Histopathologic Findings in a Case of Friedreich's Ataxia, Arch. Neurol. & Psychiat. **13**:36 (Jan.) 1925.

17. Burr, C. W.: A Contribution to the Pathology of Friedreich's Ataxia, Univ. M. Mag. **6**:598, 1893-1894.

18. Rütimeyer, L.: Ueber hereditäre Ataxia: Ein Beitrag zu den primären combinierten Systemerkrankungen des Rückenmarkes, Virchows Arch. f. path. Anat. **110**:215, 1887.

19. Bonnus, L.: Un cas de maladie de Friedreich à debut tardif: Autopsie, Nouv. iconog. de la Salpêtrière **11**:178, 1898.

with those of the spinal cord, as seen in Friedreich's disease. They were, for instance, present in the cases reported by Harris and me,[7] Menzel,[20] Arndt,[21] Thomas and Roux [22] and Switalski.[23]

One is thus justified in claiming that the forms of ataxia of Marie and Friedreich may be combined, but not in stating that they are one disease process. If they were the same morbid condition, as was maintained by Raymond [24] and others, the changes one observes in Marie's ataxia (in the medulla, pons and cerebellum) would occasionally be present also in Friedreich's disease. However, this is not the case. Raymond [24] alone mentioned olivopontocerebellar changes in his first case, in which the condition should be considered as a combined rather than as a pure type Friedreich's disease. The main difference between the two forms under discussion is histologic. As has been emphasized elsewhere,[25] the change in Marie's ataxia is degeneration of the cell bands of Essick—the ganglion cells of the medullary olives and the arciform and pontile nuclei—with secondary degeneration of the middle cerebellar peduncles (pontile brachia). In Friedreich's ataxia not the cell bands but the pathways from the spinal cord to the cerebellum (inferior cerebellar peduncles) are affected, and in late stages they are combined with degeneration of the pyramidal fibers. One is a primary nuclear disease process, such as are amyotrophic lateral sclerosis and sclerotic atrophy of the cerebellum; the other is a primary disease of the nerve fibers of the white substance of the spinal cord, as is the case in subacute combined degeneration of the cord and multiple sclerosis. As the lesion in both morbid states is in the cerebellar pathways, the main clinical phenomenon is the same—ataxia. Probably the nystagmus should be explained on the same basis—a lesion of the vestibulospinal tract, as suggested by Estable,[13] with secondary involvement of the vestibulocerebellar pathways. Other centripetal connections may also explain disturbances of speech, which are often observed in Friedreich's disease. The changes in the posterior roots are evidently retrograde—

20. Menzel, P.: Beitrag zur Kenntnis der hereditären Ataxie und Kleinhirnatrophie, Arch. f. Psychiat. **22**:160, 1890.

21. Arndt, Max: Zur Pathologie des Kleinhirns, Arch. f. Psychiat. **26**:404, 1894.

22. Thomas, André, and Roux, J. C.: Sur une forme d'hérédo-ataxie cérébelleuse, Rev. de méd., Paris **21**:762, 1901.

23. Switalski: Sur l'anatomie pathologique de l'hérédo-ataxie cérébelleuse, Nouv. iconog. de la Salpêtrière **14**:373, 1901.

24. Raymond, F.: Maladie de Friedreich et hérédo-ataxie cérébelleuse, Nouv. iconog. de la Salpêtrière **18**:5 and 121, 1905.

25. Hassin, George B.: Marie's Ataxia (Olivopontocerebellar Atrophy): Clinical and Pathologic Considerations, Arch. Neurol. & Psychiat. **37**:1371 (June) 1937. Hassin and Harris.[7]

secondary to degeneration of the posterior columns, for, as has been mentioned, they in no way differ from those exhibited in secondary degeneration of peripheral nerves.

CONCLUSIONS

1. The pathologic feature of Friedreich's disease is degeneration of the posterolateral columns of the spinal cord, which is usually seen in subacute combined degeneration of the cord. The differences in the changes in the two diseases are quantitative and are due to the time element; one is chronic degeneration, and the other, subacute.

2. The medulla, pons and cerebellum are not involved in Friedreich's disease but are affected in Marie's ataxia.

3. Lesions observable in the spinal cord in Friedreich's disease often occur in Marie's form, but the olivopontocerebellar changes so typical of the latter do not occur in the former.

4. Friedreich's and Marie's ataxia are different morbid conditions; the one is a disease of certain tracts of nerve fibers, and the other, of certain groups of ganglion cells.

5. The degeneration of the posterior roots which often occurs in cases of Friedreich's disease of long standing is secondary to that of the posterior columns, in which it is primary.

MINERALS IN NORMAL AND IN PATHOLOGIC BRAIN TISSUE, STUDIED BY MICRO-INCINERATION AND SPECTROSCOPY

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AND
ABRAHAM MYERSON, M.D.
BOSTON

The micro-incineration method (Raspail,[1] Policard[2] and Scott[3]), although not giving exact quantities, presents certain data concerning the relative distribution of ash in various parts of the normal nervous system (Scott[3a] and Alexander and Myerson[4]) and in various types of lesions in the pathologic nervous system (Alexander and Myerson[4]).

On the micro-incinerated slide normal gray matter appears rich, while normal white matter appears poor in ash (fig. 1). Allocortical areas (fig. 2 *A* and *B*) and the cerebellar cortex[5] are richer in mineral ash than isocortical areas of the cerebral cortex (fig. 2 *A*). Cell groups in the process of development are richer in mineral ash than the same areas after complete differentiation, as can be demonstrated in the cerebellar cortex and the area striata (Alexander[6]).

These gross differences are explained by differences in mineral distribution in the various parts of the neuron itself. A ganglion cell contains rich deposits of ash in the nucleolus and the tigroid bodies (fig.

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From the Division of Psychiatric Research, the Boston State Hospital, and the Department of Neurology, Harvard University Medical School.

1. Raspail, F. V.: Nouveau système de chimie organique, fondé sur des méthodes nouvelles d'observation, Paris, J.-B. Baillière, 1833, p. 528.

2. Policard, A.: Sur une méthode de microincinération applicable aux récherches histochimiques, Bull. Soc. chim. biol. **33**:1551, 1923.

3. Scott, G. H.: (*a*) The Localization of Mineral Salts in Cells of Some Mammalian Tissues by Micro-Incineration, Am. J. Anat. **53**:243, 1933; (*b*) A Critical Study and Review of the Method of Microincineration, Protoplasma **20**: 133, 1933.

4. Alexander, L., and Myerson, A.: The Mineral Content of Various Cerebral Lesions as Demonstrated by the Microincineration Method, Am. J. Path. **13**:405, 1937.

5. Alexander and Myerson,[4] figures 6 and 9.

6. Alexander, L.: The Neurone as Studied by Micro-Incineration, Anat. Rec. (supp. 3) **67**:3, 1937.

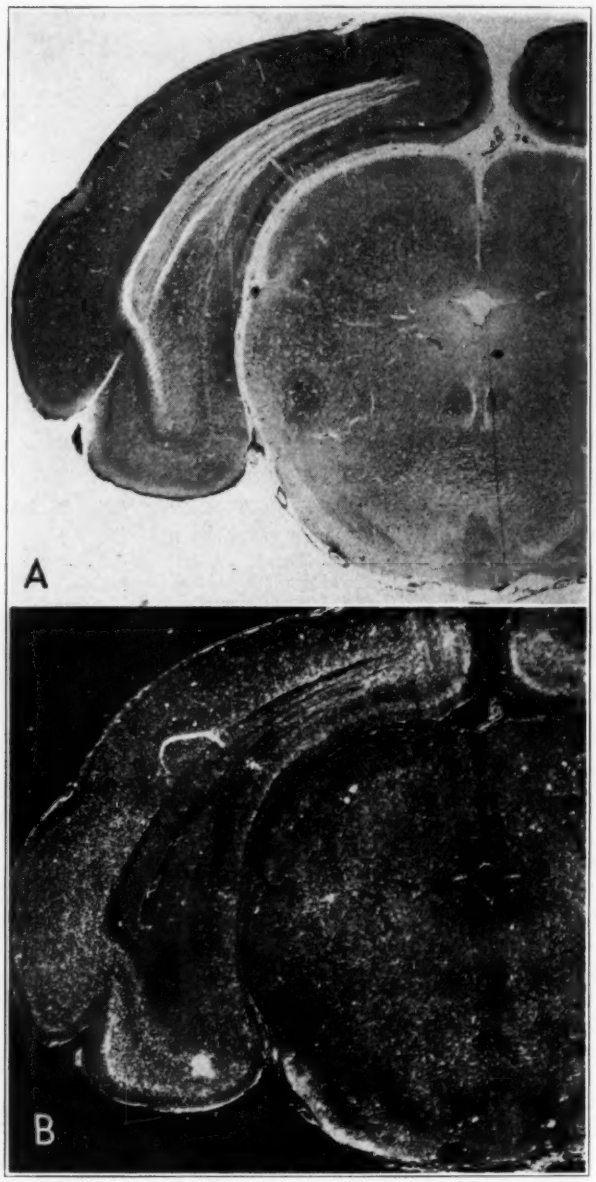

Fig. 1.—Sections (× 8) through the left occipitoparietal lobe and the midbrain of the guinea-pig. *A*, hematoxylin-eosin stain. *B*, section neighboring that seen in *A*; micro-incineration; oblique transillumination. Note the richer ash residue of the cortical gray matter than that of the white matter of the occipitoparietal lobe.

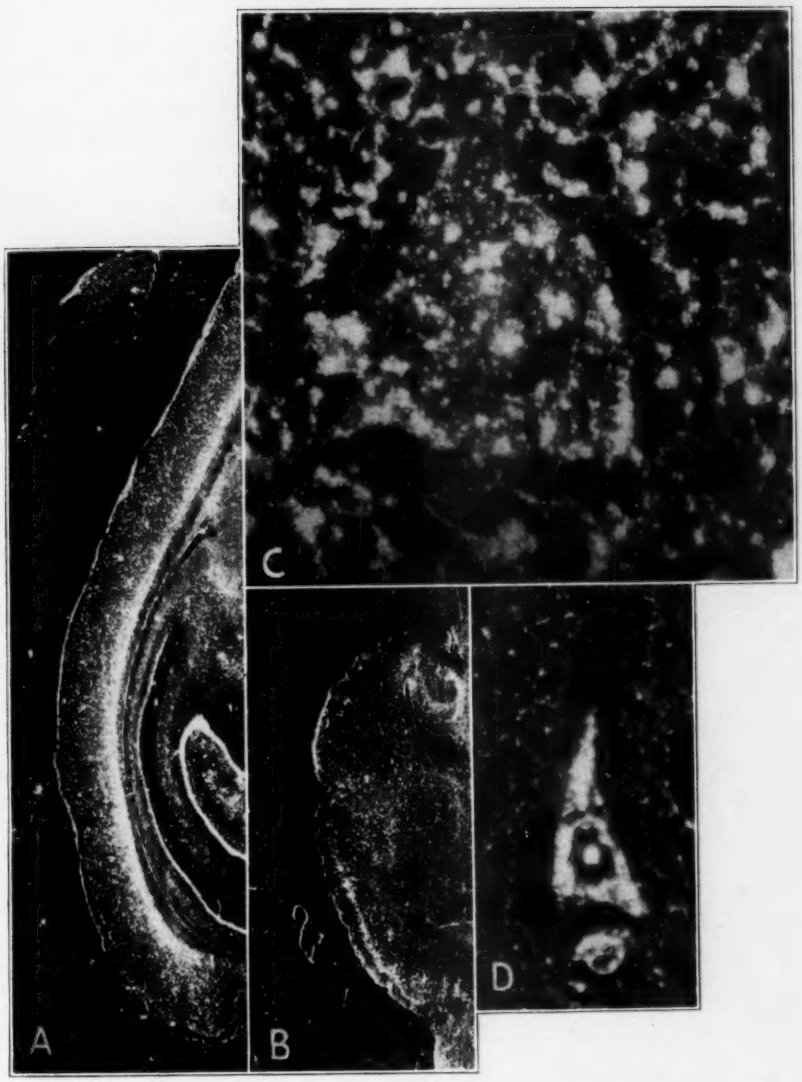

Fig. 2.—Micro-incineration preparations; oblique transillumination. *A* (×8), section through the cornu ammonis and temporoparietal lobe of the rabbit. Note the richer ash residue in the fascia dentata than that in the isocortical areas of the temporoparietal lobe. *B* (×8), cornu ammonis, area entorhinalis and area praepyriformis of the rabbit. Note the rich ash residue in the cornu ammonis and the prepyriform area. *C* (×760), anterior horn cell in the cat. Note the rich ash content of the tigroid bodies and nucleolus, the nucleus being essentially free from ash except for some fine strands, especially along the nuclear membrane. *D* (×760), ganglion cell from the cornu ammonis in man. Note the ash residue corresponding to the tigroid bodies and nucleolus, the nucleus being essentially free from ash except for some fine strands, especially along the nuclear membrane.

2 *C* and *D*), while the normal intracellular neurofibrillae and the axis-cylinder contain little or no mineral ash (Scott [3a] and Alexander and Myerson [4]). The myelin sheath contains small amounts of ash corresponding to the myelo-axostroma of Kaplan, while the lipoid of the myelin sheath is free from mineral ash (Alexander [6]).

Of the pathologic states, such lesions as hemorrhages, inflammation and tumor (fig. 3), the cell disease of tuberous sclerosis and the

Fig. 3.—Metastasis to the brain from a carcinoma of the bronchial epithelium, in man (micro-incineration; dark field illumination; × 110). Note the richer ash residue of the tumor nodule (upper half of figure) than that in the surrounding brain tissue (lower half of figure).

fibrillary strands in Alzheimer's cell disease are characterized by hypermineralization, while the foci of ischemic necrosis and softening, the depleted layers and areas of cortical atrophy in Pick's focal senile atrophy, the plaques of multiple sclerosis and the cell disease in amaurotic idiocy are characterized by demineralization (Alexander and Myerson [4]).

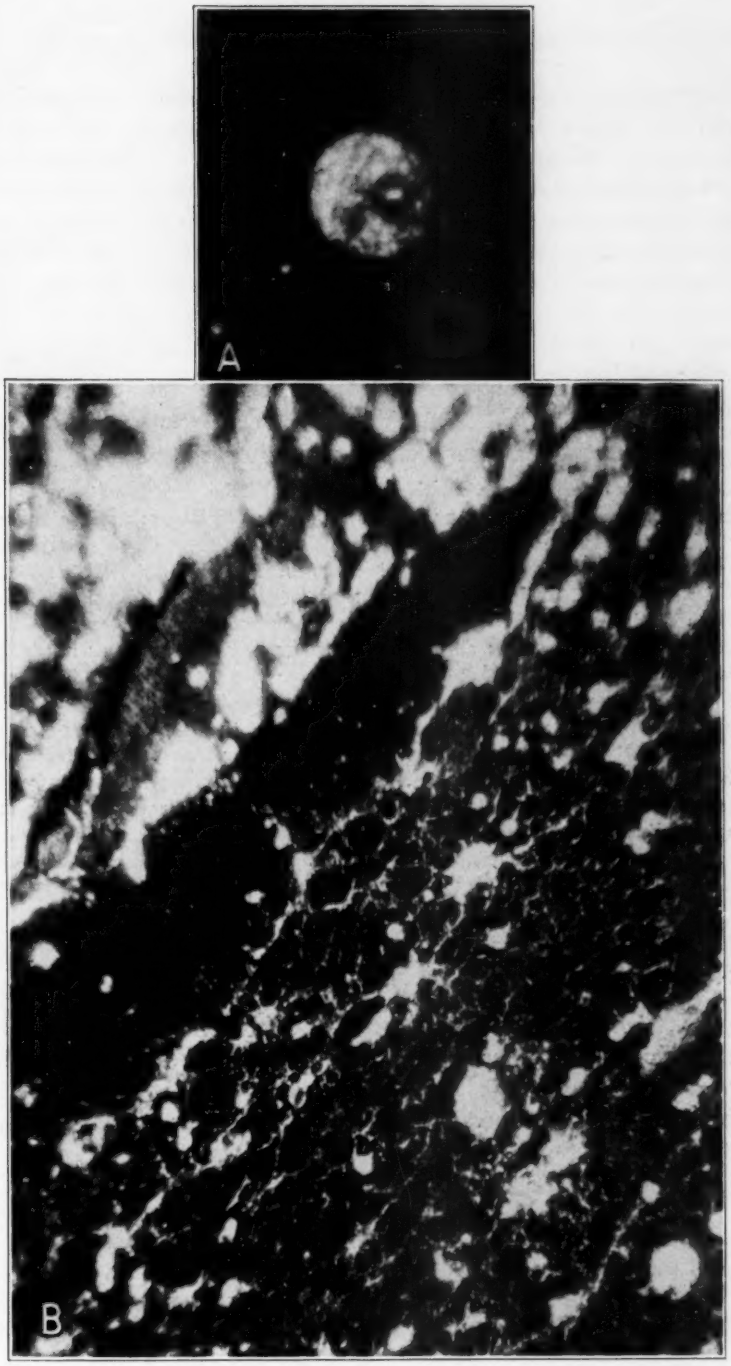

Fig. 4.—*A* (× 760) perivascular histiocyte from a plaque of multiple sclerosis, loaded with mineral granules containing iron oxide, and *B* (× 500), protoplasmic glial astrocytes and perivascular infiltration from a plaque of multiple sclerosis (micro-incineration; dark field illumination). Note the rich mineral content of the astrocytes and the perivascular infiltrative cells, in contrast to the demineralized background.

Demineralization in vascular lesions and in those of multiple sclerosis, however, affects only the parenchyma, while the remainder of the vascular network, the scavenger cells and the proliferating glial elements stand out as hypermineralized structures against the demineralized background of the tissue. This is especially well demonstrated by the proliferating astrocytes in plaques of multiple sclerosis (fig. 4*B*). In the plaques of multiple sclerosis and the tissue immediately surrounding the plaque, large perivascular histiocytes are seen which, apart from lipoid and some whitish and bluish ash, contain large amounts of iron oxide (fig. 4*A*). Senile plaques show neither excess nor deficit of mineral ash.

SPECTROSCOPIC METHOD

In order to determine the relative proportions of the various minerals in these changes, we have subjected tissue from pathologic material, such as we studied in our micro-incineration work,[4] to spectroscopic analysis.[7] (These determinations were made through the generous collaboration of Prof. George R. Harrison, Mr. David Richardson and Mr. Rockwell Kent, of the department of physics, the Massachusetts Institute of Technology.) Thirty-seven normal and pathologic areas were examined in fourteen cases; altogether, the emission spectra of four hundred and eighty-three samples were photographed and nine elements determined. For each sample, the iron was first determined by the increase in intensity of the lines for iron produced on the addition of a known amount of iron to a weighed amount of the sample. By relating the intensity of the lines for iron to the intensities for each of the other elements studied, it is possible by reference to previously determined calibration curves to estimate the amount of the element present in the sample. This method requires little material and makes possible a number of determinations of different elements after the necessary working curves have been obtained. With experience and careful manipulation the method yields reproducible results with adequate precision.

RESULTS OF INVESTIGATION

Normal Gray and White Matter of the Cerebral Cortex of the Human Adult.—The normal gray matter of the cerebrum of the human adult contained 81.75 per cent water and 18.25 per cent solids, and the normal white matter, 70.45 per cent water and 29.55 per cent solids. The minerals of the normal gray and white matter are given in percentages of the weight of the dried and the fresh tissue:

	Sodium	Potassium	Phosphorus	Copper	Iron	Calcium	Magnesium	Manganese	Lead
Normal gray matter (percentage of dry weight)....	0.21	0.056	0.98	0.0060	0.031	0.021	0.98	0.00016	0
Normal white matter (percentage of dry weight)....	0.10	0.040	1.80	0.0057	0.021	0.011	0.55	0.00020	0
Normal gray matter (percentage of fresh tissue)....	0.0384	0.01023	0.179	0.001097	0.00565	0.00384	0.179	0.0000292	0
Normal white matter (percentage of fresh tissue)....	0.02955	0.01180	0.532	0.001685	0.00620	0.00325	0.1625	0.0000592	0

7. Gerlach, W., and Schweitzer, E.: Foundations and Methods of Chemical Analysis by the Emission Spectrum, London, Adam Hilger, Ltd., 1929. Gerlach, W., and Gerlach, W.: Clinical and Pathological Applications of Spectrum Analysis, translated by Joyce Hilger Twyman, London, Adam Hilger, Ltd., 1934.

These figures at present should be regarded as proportions rather than as absolute weights. The determination of absolute weights on a still larger amount of material is thus necessary. When, therefore, one limits oneself to proportions, it appears from this table that the white matter contains about twice as much phosphorus as the gray, while the gray matter is richer in sodium, calcium and magnesium. The dried substance of the gray matter is richer in iron, while potassium, manganese and copper are about evenly distributed. These relationships are well illustrated by figure 5.

Cerebral Cortex of the New-Born Infant.—The ash of the gray matter of the cortex in the normal new-born human infant contained twice as much potassium, four and one-half times as much sodium, twice

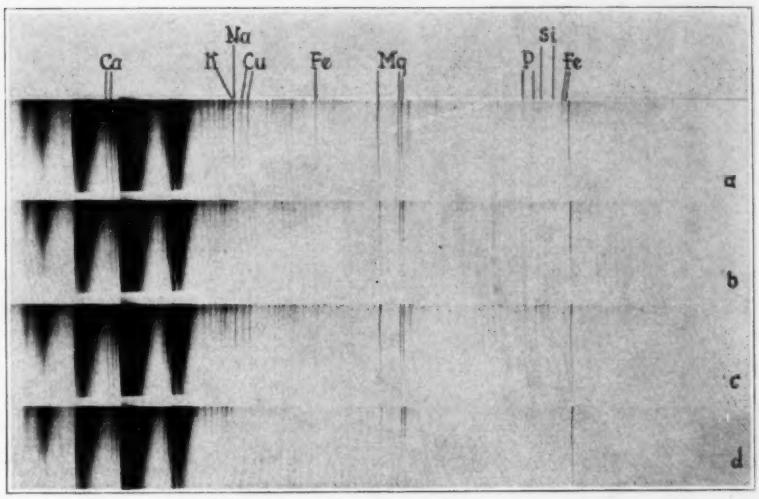

Fig. 5.—Emission spectra for the normal gray and white matter (case 1); 10 amperes $\mp$; disk set low. (*a*) Normal gray matter, charred tissue corresponding to 20 mg. of dried tissue, sixty seconds; (*b*) same as *a*, thirty seconds; (*c*) normal white matter, 20 mg. of dried tissue, sixty seconds; (*d*) same as *c*, thirty seconds. Note the longer lines for sodium, calcium, magnesium and iron in the normal gray matter and the longer lines for phosphorus in the normal white matter.

as much magnesium, about as much calcium and phosphorus, but only three-fifths as much iron as the gray matter in the normal adult. The ash of the white matter of the brain of the normal new-born contained three times as much potassium as that of the normal adult, four and one-half times as much sodium, twice as much calcium and magnesium and about three-fifths as much iron (fig. 6).

Foci of Softening.—In early foci of softening, the diseased gray matter showed about one-half the potassium value for normal gray matter from the same brain and a significant loss of phosphorus, while the amount of iron was increased to more than twice that of normal gray matter. Sodium also showed a significant rise (fig. 7*A*).

The white matter in early softening, as compared with normal white matter from the same brain, showed a significant elevation in the iron, magnesium and sodium contents and loss in potassium to about one seventh of the original amount, while phosphorus remained remarkably constant (fig. 7*B*).

The water content of the gray matter in the early foci of softening was 83.16 per cent, and the solids, 16.8 per cent. In early softening of

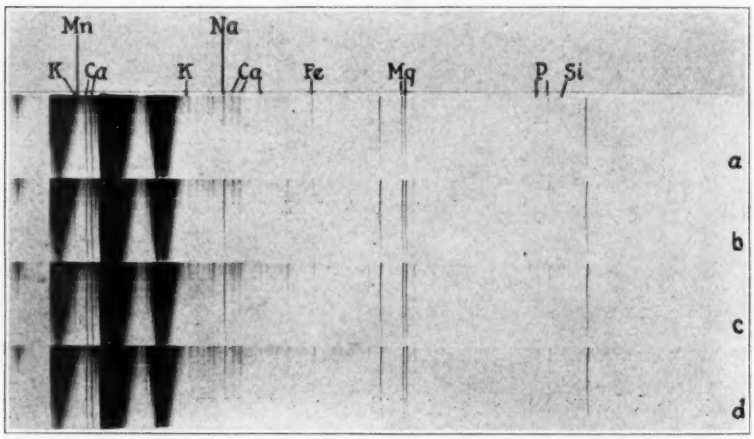

Fig. 6.—Emission spectra for the gray and white matter of a new-born infant (case 8) as compared with those for the brain of the adult (case 1); exposure one minute and thirty seconds. (*a*) Mixture of normal gray and white matter of the human adult, 10.5 mg. of charred tissue; (*b*) gray matter of the new-born infant, 9.8 mg. of charred tissue; (*c*) white matter of the new-born infant, 10.3 mg. of charred tissue; (*d*) mixture of normal gray and white matter of the human adult, 9.8 mg. of charred tissue. Note the longer lines for potassium, sodium and magnesium and the shorter lines for iron in the brain of the new-born.

the white matter the water content was 79.13 per cent, and the solids, 20.87 per cent.

In an older vascular lesion, in which there was considerable reparative gliosis, the water content of the softened gray matter was 88.62 per cent, and the solids, 11.38 per cent. The water content of normal gray matter from the analogous site in the other hemisphere was 83.09 per cent, and the solids, 16.91 per cent. The water content of the softened white matter was 85.62 per cent, and the solids, 14.38 per

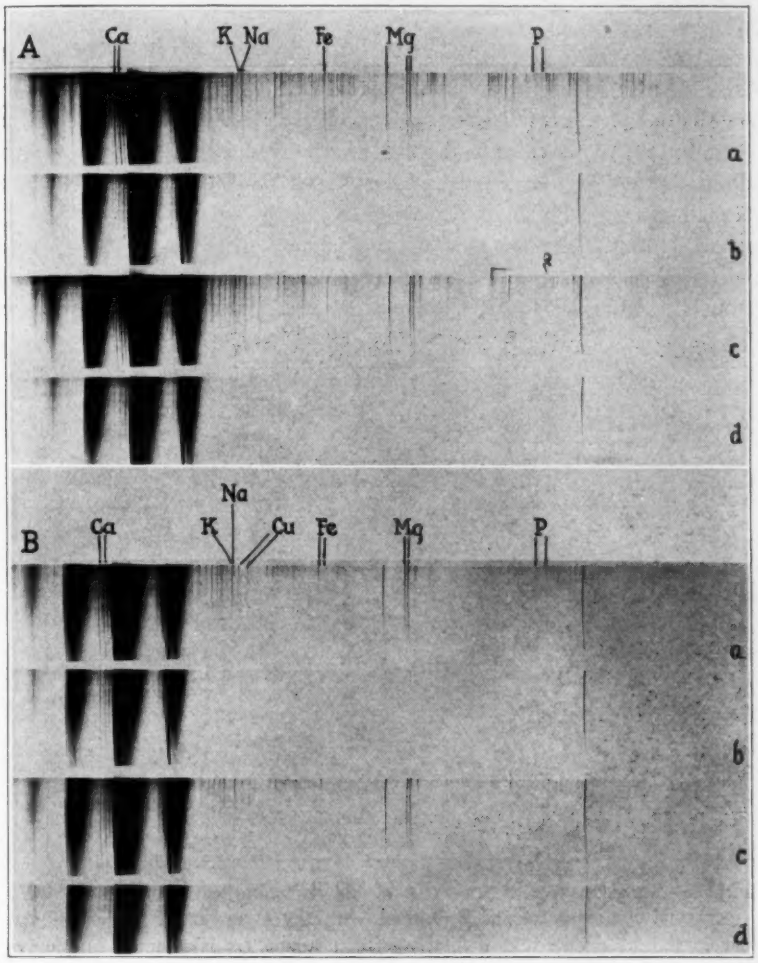

Fig. 7.—*A*, emission spectra for early softening of the gray matter as compared with those for normal gray matter (case 1); disk down. (*a*) Softened gray matter, 20 mg. of dried tissue, three minutes; (*b*) same as *a*, thirty seconds; (*c*) normal gray matter, 20 mg. of dried tissue, three minutes; (*d*) same as *c*, thirty seconds. Note the longer lines for iron and sodium of the softened gray matter (*a*) than of the normal gray matter (*c*). *B*, emission spectra for early softening of the white matter as compared with those for normal white matter (case 1); disk down. (*a*) Softened white matter, 20 mg. of dried tissue, two minutes; (*b*) same as *a*, thirty seconds; (*c*) normal white matter from the same brain, 20 mg. of dried tissue, two minutes; (*d*) same as *c*, thirty seconds. The lines for iron, magnesium and sodium are longer for the softened white matter, while the lines for phosphorus are equal.

cent; the water content of normal white matter in the same case was 75.7 per cent, and the solids, 24.3 per cent. In the softened white matter in this case (fig. 8, row *b*), the amount of iron was twice that of the normal white matter in the same case (fig. 8, row *e*), and there was about twice as much potassium as in the normal white matter. The amounts of calcium and magnesium were equal to normal, while sodium was slightly decreased. Phosphorus was not diminished. In the softened gray matter in the same case (fig. 8, row *a*), the amount of iron was about equal to that of the normal gray matter in the same case (fig. 8, row *d*), while there were about three and one-half times as much calcium, three times as much potassium and one-half as much

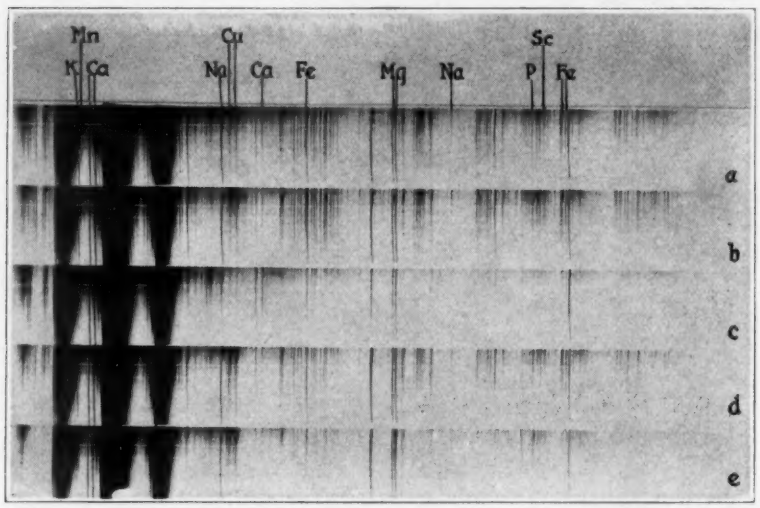

Fig. 8.—Emission spectra for areas of old softening with reparative gliosis in the gray and white matter as compared with those for normal gray and white matter in the same case and with those for a tumor (meningioma) of the brain; one minute; disk up. (*a*) Old softening with reparative gliosis in the gray matter (case 9), 9.1 mg. of charred substance; (*b*) old softening with reparative gliosis in the white matter (case 9), 8 mg. of charred substance; (*c*) tumor of the brain, meningioma (case 12), 10.8 mg. of charred substance; (*d*) normal gray matter in case 9, 10.2 mg. of charred substance; (*e*) normal white matter in case 9, 10.3 mg. of charred substance. Note the greater amount of calcium in the tumor (*c*), which exceeds both that of the normal gray and white matter and that of areas of old softening with reparative gliosis. Note also the excess of iron, calcium and potassium in the old softening of the gray and white matter as compared with that for normal gray and white matter in the same case.

phosphorus as in the normal gray matter in the same case. The magnesium and sodium contents were about equal to normal. The relatively greater amount of calcium and potassium in this case apparently corresponds to the advanced gliosis.

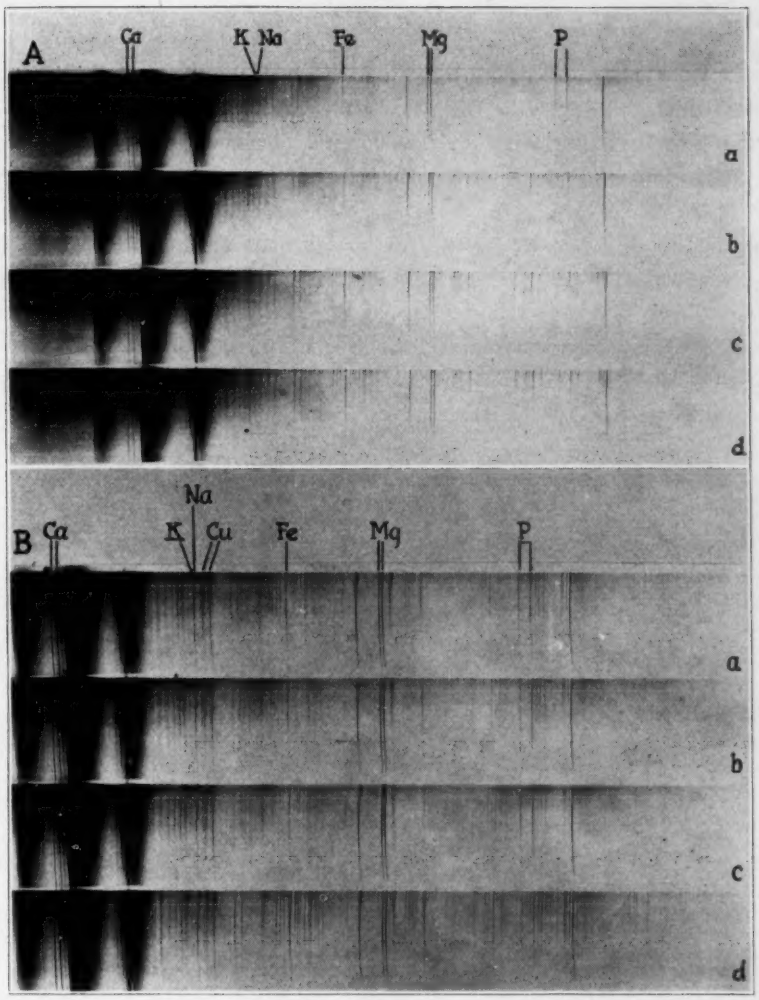

Fig. 9.—*A*, emission spectra for softened white and gray matter from charred material corresponding to 20 mg. of dried tissue (case 1); two minutes; disk down. (*a*) Softened white matter, 13.9 mg. of charred tissue; (*b*) same as *a*, but with the addition of 5 micrograms (gamma) of iron; (*c*) softened gray matter, 13.3 mg. of charred tissue; (*d*) same as *c*, but with the addition of 5 micrograms of iron. Note the similarity in the proportions of minerals in the softened white and gray matter to the relative proportions for normal white and gray matter, the lines of iron, sodium, calcium and magnesium being longer in the gray matter and the lines for phosphorus longer in the white matter. *B*, emission spectra for normal and softened gray and white matter; (case 1) 40 seconds; disk up. (*a*) Mixture of normal gray and white matter, 13.5 mg. of charred tissue; (*b*) softened white matter, 13.6 mg. of charred tissue; (*c*) same as *b*, 13 mg., with the addition of 0.42 micrograms of manganese; (*d*) softened gray matter, 12.7 mg. of charred tissue. Note the longer lines for iron of both the softened gray and the softened white matter as compared to those of a mixture of normal gray and white matter. Note also the longer lines for calcium, sodium and iron of softened gray matter and the longer lines for phosphorus of softened white matter.

It is of interest to note that in early softening the relative proportions of the elements in the gray and those in the white matter are remarkably constant (fig. 9). The main differences appear when either is contrasted with values for normal material (fig. 10).

Multiple Sclerosis.—In three cases the plaques of multiple sclerosis showed about twice as much iron as normal white matter from the same or other brains and only slightly less iron than the gray matter from the same brain (figs. 11 and 12). In two of these cases, however, the grossly normal gray matter also showed slightly more iron than the gray matter from presumably normal brains. In one case the amount was equal to normal. We cannot exclude the possibility that

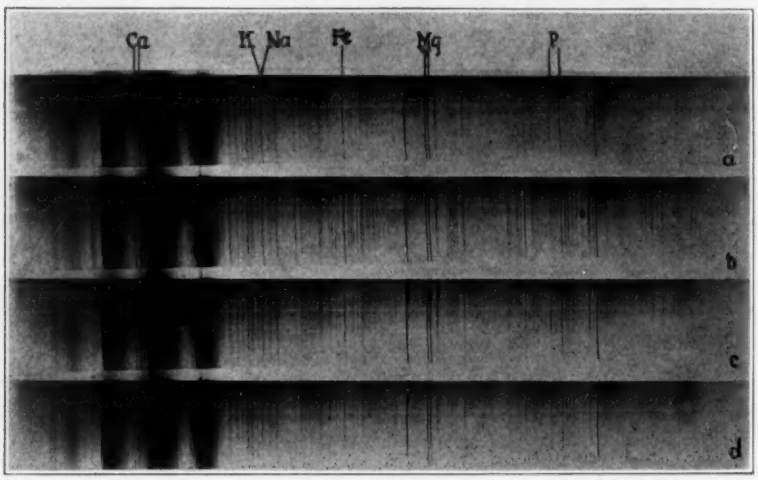

Fig. 10.—Emission spectra for normal and softened gray and white matter from charred material corresponding to 40 mg. of dried tissue (case 1); ninety seconds; disk up. (*a*) Softened white matter; (*b*) softened gray matter; (*c*) normal gray matter; (*d*) normal white matter. Note the similarity in the proportions of elements in early softening of gray and white matter as compared with the proportions of elements in normal gray and white matter and the strong lines for iron in both the softened gray and the softened white matter as compared with those for normal gray and white matter.

in the two cases in which the iron content of the gray matter was increased there may actually have been some of the small lesions in the cortical gray matter which are not uncommon in this disease. Aside from a decrease in calcium in the plaques, in one case to about one-half the normal value, the other elements, especially phosphorus, showed no significant alterations in the lesions of multiple sclerosis.

Dementia Paralytica.—In the one case studied there was a slight increase of iron in the white matter, as compared with the gray matter in the same case (fig. 13), but a definite decrease in the gray as well as the white matter, as compared with our normal controls. This tends to indicate that the loss of iron in dementia paralytica by decrease of

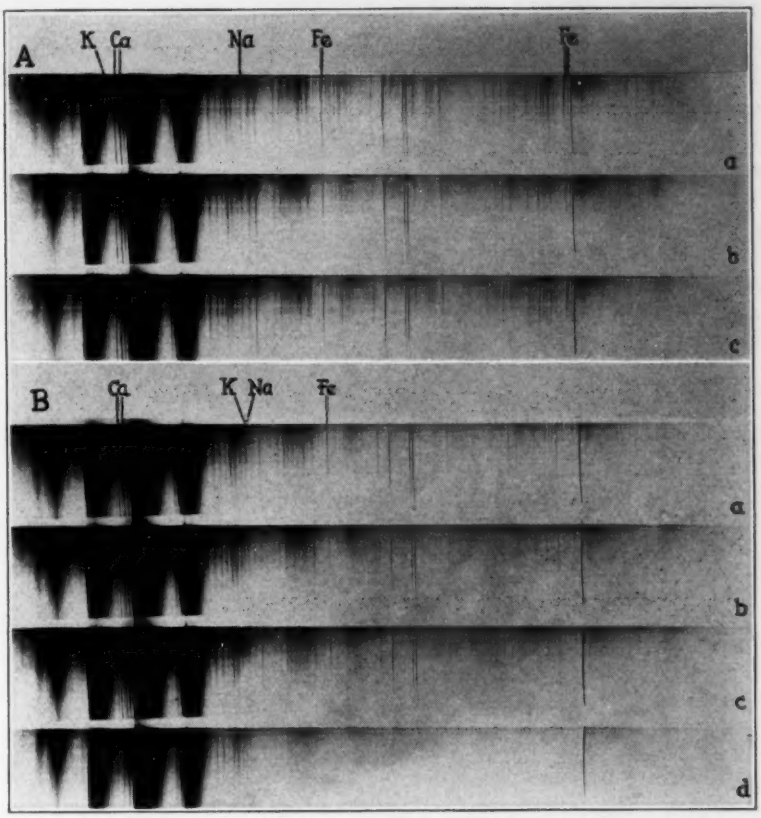

Fig. 11.—Emission spectra for plaques of multiple sclerosis (case 5) as compared with those for normal white and gray matter in the same case. *A*, 40 mg. of dried tissue; ninety seconds; disk up. (*a*) Plaques of multiple sclerosis; (*b*) normal white matter in the same case; (*c*) normal gray matter in the same case. *B*, 20 mg. of dried substance; 10 amperes $\mp$; disk down. (*a*) Plaque of multiple sclerosis, three minutes; (*b*) normal white matter from the same brain, three minutes; (*c*) normal gray matter from the same brain, three minutes; (*d*) same as *c*, one minute. Note the longer line for iron of the plaque than that of the normal white matter in the same case.

the volume of the vascular bed due to narrowing and obliteration of cerebral blood vessels is greater than the increase by perivascular and intraglial tissue deposits of iron.

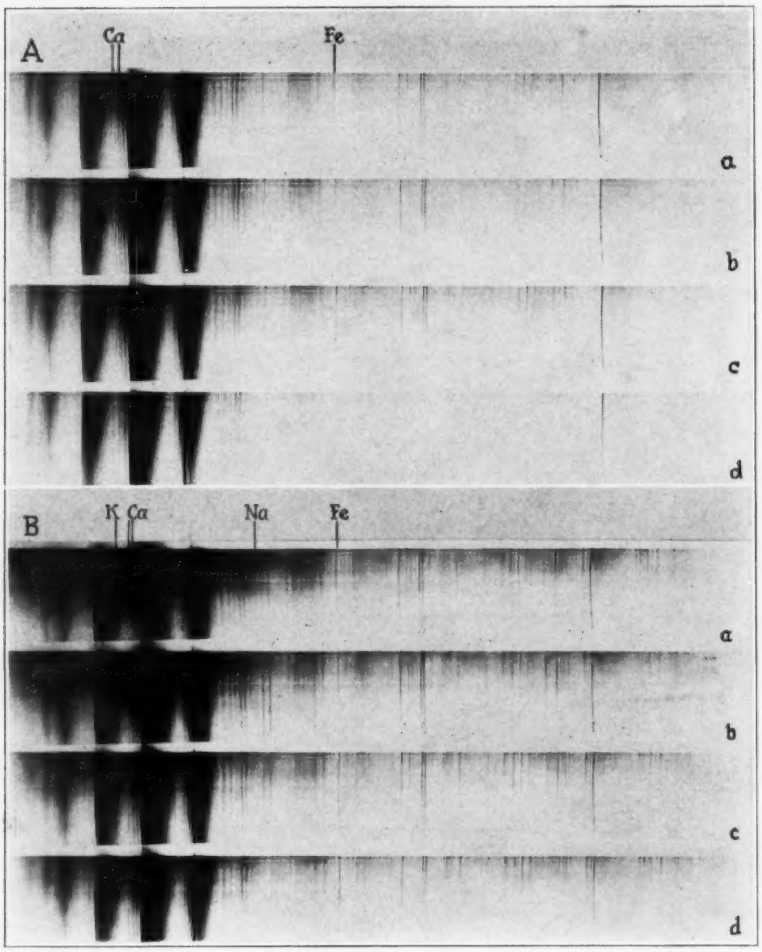

Fig. 12.—Emission spectra for plaques of multiple sclerosis as compared with those for normal white and gray matter from the same brain (case 4). *A*, 20 mg. of dried substance; 10 amperes $\mp$; disk down. (*a*) Plaques of multiple sclerosis, three minutes; (*b*) normal white matter in the same case, three minutes; (*c*) normal gray matter in the same case, three minutes; (*d*) same as *c*, one minute. *B*, 40 mg. dried substance; disk up. (*a*) Plaques of multiple sclerosis, ninety seconds; (*b*) normal white matter from the same brain, ninety seconds; (*c*) normal gray matter from the same brain, ninety seconds; (*d*) same as *c*, one minute. Note the longer line for iron in the plaques, which exceeds that of the normal white matter and slightly that of the normal gray matter in the same case.

Lead Encephalitis.—In the one case studied, that of a child aged 3 years, the amount of lead in the gray matter was 0.0017 per cent of the dried tissue, and that in the white matter, 0.00078 per cent. The amount of lead, therefore, was 2.61 times as great in the gray as in the white matter (fig. 14). The calcium was diminished in both the gray and the white matter, the gray containing 0.007 per cent and the white 0.006 per cent of the dried substance. As compared with the normal, the relative loss was greater in the gray matter. The iron was greatly diminished in both the gray and the white matter—relatively much more in the gray. The gray matter contained 0.009 per cent, and the white, 0.013 per cent of iron in its dried substance. Figure

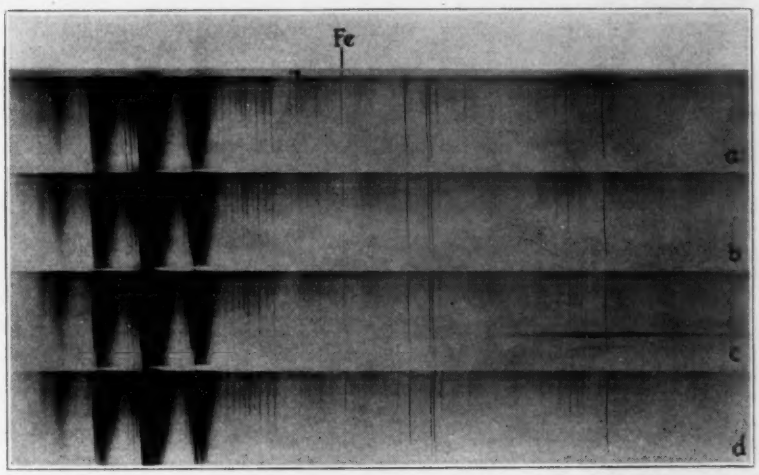

Fig. 13.—Emission spectra for the gray and white matter in a case of dementia paralytica as compared with those for normal gray and white matter; forty seconds; disk up. (*a*) Mixture of normal gray and white matter, 12 mg. of charred substance; (*b*) white matter in a case of dementia paralytica, 11.4 mg. of charred substance; (*c*) white matter in a case of dementia paralytica, 11.2 mg. of charred substance, with the addition of 0.34 micrograms of manganese; (*d*) gray matter in a case of dementia paralytica, 8.6 mg. of charred substance. Note the relatively slight difference in the lines for iron between the gray and the white matter in the case of dementia paralytica as compared with the difference in normal brains (compare figure 5).

15 *A* illustrates the remarkable loss of iron as compared with that of normal tissue, and figure 15 *B* shows the rapprochement of the length of the lines for iron both in the gray and in the white matter in this condition. There is practically no difference between the gray and the white matter as to the iron content. There were a great deal of cerebral edema in this case, flattening of the convolutions and gross anemia,

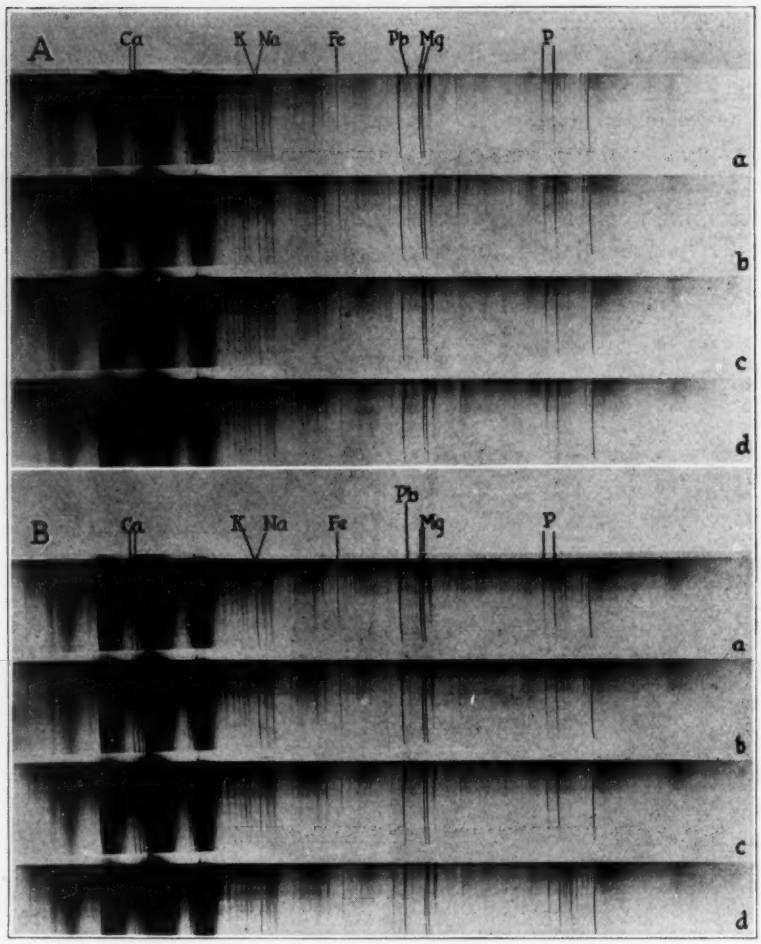

Fig. 14.—Emission spectra for gray and white matter in a case of lead encephalitis in a 3 year old child. *A*, exposure of thirty seconds; disk up. (*a*) Gray matter in a case of lead encephalitis, 10.4 mg. of charred substance (corresponding to 100 mg. of fresh tissue); (*b*) same as *a*, with the addition of 0.5 micrograms (gamma) of lead; (*c*) white matter in a case of encephalitis, 12.8 mg. of charred tissue (corresponding to 100 mg. fresh tissue); (*d*) same as *c*, with the addition of 0.5 micrograms of lead. Note the much longer line for lead in the gray than in the white matter in the same case. *B*, spectra in another exposure. (*a*) Gray matter, 10.4 mg. charred substance (corresponding to 100 mg. fresh tissue); (*b*) same as *a*, with the addition of 0.5 micrograms of lead; (*c*) white matter, 12.8 mg. charred substance (corresponding to 100 mg. fresh tissue); (*d*) same as *c*, with the addition of 0.3 micrograms of lead. Note the excess of lead in the gray as compared with the white matter.

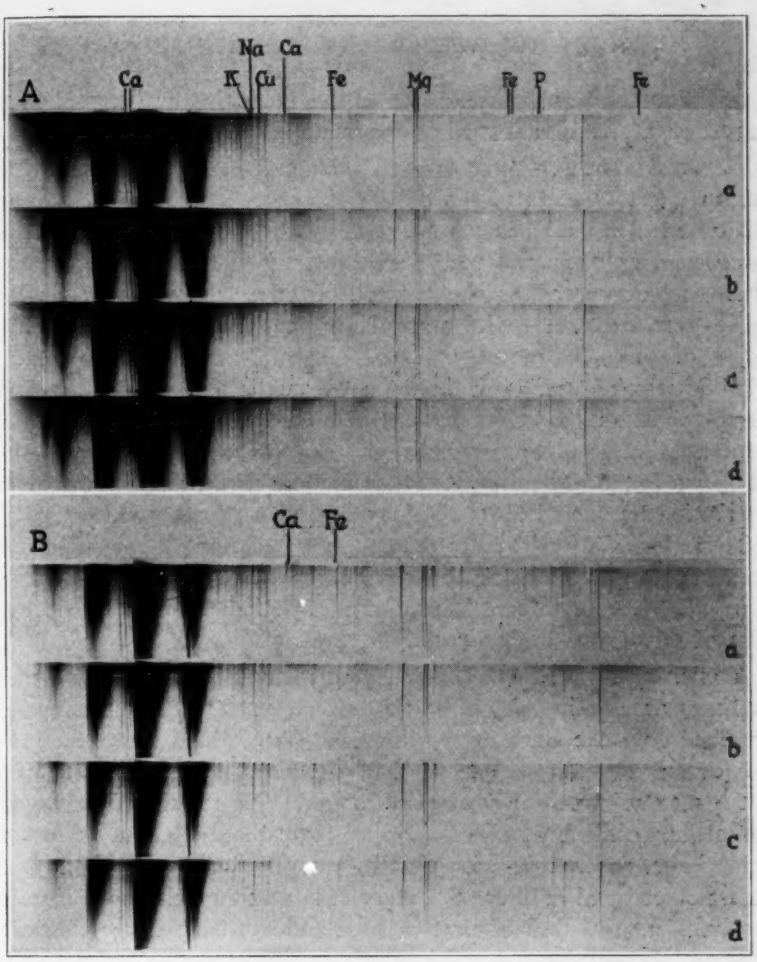

Fig. 15.—*A*, emission spectrum for the gray matter in a case of lead encephalitis (case 6) compared with the spectra for the normal gray and white matter in case 1, studied for its relative content of iron; two minutes; disk down. (*a*) Mixture of normal gray and white matter in case 1 (human adult), 12.2 mg. of charred tissue; (*b*) gray matter in a case of lead encephalitis, 10 mg. of charred tissue; (*c*) gray matter in a case of lead encephalitis, 11 mg. of charred tissue, with the addition of 5 micrograms (gamma) of iron; (*d*) gray matter in case of lead encephalitis, 4.8 mg. of charred tissue, with the addition of 5.9 mg. of charred mixture of normal gray and white matter in case 1. Note the shortness of the line for iron in the gray matter in the case of lead encephalitis. *B*, emission spectrum for the gray and for the white matter in a case of lead encephalitis in a 3 year old child (case 6) compared with each other and with the spectrum for a mixture of normal gray and white matter (case 1); forty seconds; disk up. (*a*) Mixture of normal gray and white matter in case 1, 13.6 mg. of charred tissue; (*b*) gray matter in a case of lead encephalitis, 10.6 mg. of charred substance; (*c*) same as *b*, 12.1 mg. of charred tissue, with the addition of 0.48 micrograms of manganese; (*d*) white matter in a case of lead encephalitis, 13 mg. of charred substance. Note the shortness of the lines for calcium and iron in the gray and white matter in the case of lead encephalitis as compared with those for the mixture of normal gray and white matter in case 1.

especially of the gray matter, while the white matter showed slight congestion in places and rare perivascular hemorrhages.

Cerebral Edema.—In a case of unilateral cerebral edema (hemiedema) due to abscess of the brain on the same side, the sodium and calcium were increased in the gray and white matter of the edematous hemisphere, as compared with the values for the normal right hemisphere, which served as the control. In the edematous hemisphere sodium was increased to 1.4 times the normal value in the gray matter and to 2.5 times the normal value in the white matter, and calcium, to 1.8 times the normal value in the gray matter and to 3.6 times the normal value in the white matter. Iron was increased to 1.8 times the normal value in the gray matter, while quantitative changes were not shown in the white matter. These findings throw light on a previous observation by one of us (L. A.[8]), namely, that in cerebral edema the white matter is affected more than the gray matter. It may also offer a tentative explanation for the observation made by Looney and one of us (L. A.[9]) that there is an increase post mortem in the isotonic point of edematous brain tissue.

Tumor of the Brain.—The ash of a meningioma was found to be ten times as rich in calcium as the normal gray matter. However, it contained only one sixth of the iron, one sixteenth of the sodium, one fifth of the phosphorus, one third of the potassium and one fifteenth of the magnesium of normal gray matter. The striking difference in the calcium content of this tumor as compared with that of normal brain tissue, as well as with that of organized old softening of the brain, is illustrated in figure 8. The ash of a spongioblastoma of mixed type, with a great deal of protoplasmic and fibrillary astrocytic differentiation, showed more potassium but less magnesium and less than half the phosphorus content of normal gray matter, while calcium, sodium and iron were evenly distributed.

SUMMARY

These spectroscopic findings demonstrate the following points:

1. The normal cerebral gray matter of the human adult is richer than the white matter in iron, calcium, magnesium and sodium, while normal white matter is richer in phosphorus.

2. The brain of the new-born human infant is richer in most elements, but poorer in iron, than that of the adult. The lowered iron

8. Alexander, L.: Cerebral Changes in Gastrointestinal Infections with Terminal Cachexia and Their Relation to Physicochemical Properties of the Brain, J. Nerv. & Ment. Dis. **81**:558, 1835.

9. Alexander, L., and Looney, J. M.: Some Physicochemical Properties of the Brain, Especially in Senile Dementia and in Cerebral Edema, to be published.

content seems to correspond to the lesser vascular density of the brain of the new-born.

3. In foci of ischemic necrosis, softening and multiple sclerosis the alteration in the spectroscopic picture is surprisingly insignificant as compared with the intensive demineralization of the tissue demonstrated by micro-incinerated preparations in these conditions. However, while the tissue itself appears demineralized in micro-incinerated preparations, ample mineral is demonstrated in hypermineralized scavenger and glia cells, which stand out against the otherwise demineralized background of these lesions. Our spectroscopic studies justify the conclusion that these scavenger and glia cells contain most of the minerals in about the proportions which normally are distributed evenly within the tissue, except for potassium, which is diminished in freshly softened areas, and for iron, which is increased in all these lesions. The iron in these lesions is probably hematogenous and points to vascular dilatation, stasis or thrombosis in the areas involved.

4. In dementia paralytica there is no absolute increase of iron. This tends to indicate that the loss of iron by decrease of the volume of the vascular bed due to narrowing and obliteration of cerebral blood vessels, especially capillaries, in this disease is greater than the increase of iron by perivascular and intraglial tissue deposits.

5. In lead encephalitis, more lead is deposited in the gray than in the white matter of the brain.

6. In edematous brain tissue, sodium and calcium are increased. This increase is relatively greater in the white than in the gray matter.

7. The ash of a meningioma was found to be ten times as rich in calcium as the normal gray matter, while the other elements were diminished. The ash of a spongioblastoma of mixed type, with a great deal of protoplasmic and fibrillary astrocytic differentiation, showed more potassium, but less phosphorus and magnesium, than the normal gray matter.

Case Reports

A CASE OF EPILEPSY

Associated with Meningioma of the Optic Nerve Sheath, Compressing the Olfactory Centers, Dural Calcifications and Thalamic Lesions

JAMES W. PAPEZ, M.D., AND R. WAYNE RUNDLES, B.A., ITHACA, N. Y.

Epilepsy may be associated with various injuries of the brain, especially those which affect the parietal or the frontal cortex. Tumors, trauma, scars, degenerations and atrophic conditions have been frequently recorded as concomitant lesions or factors predisposing to convulsive attacks. In the case reported here there were several minor lesions and areas of local atrophy of the premotor cortex on both sides. With these were degenerations of small fiber bundles between the cortex and the thalamus and a small cavity in the left thalamus.

There was a history of long-standing blindness in the right eye. The outstanding observation was a meningioma of the right optic nerve situated at the optic foramen. The tumor compressed the right olfactory region and the neighboring fiber tracts. For a time the convulsive attacks were signalized by an olfactory aura. The clinical history in the case and the variety of anatomic deficiencies associated with the lesions are recorded here.

REPORT OF CASE

History.—The patient was born in Maine, on Oct. 11, 1859, of old American-English stock. She died on March 9, 1935, at the age of 76, after suffering for years from atrophy of the optic nerve, epilepsy and, finally, a tumor of the brain. The pathologic changes associated with these clinical conditions are the subject of this report.

She received a medical degree in 1885. In the same year she was married. She had three sons and one daughter. Her personal history is that of an intelligent and enterprising woman, with increasing physical handicaps but normal cultivated interests and normal social, personal and emotional adjustments during most of her life. She practiced medicine actively for twenty-two years and intermittently for ten years more. The later part of her life was spent at home.

Her early illnesses included typhoid, scarlet fever, septicemia and chronic arthritis of the hip and knee joints. She had slight pyorrhea in youth and total extraction of teeth was done at the age of 56. When 44 she sustained a fracture of the leg. At the age of 56 she gradually became blind in the right eye, due to retrobulbar atrophy of the optic nerve. At the age of 61 (1920) she began to have periods of trembling, which soon developed into true epileptic seizures.

In August 1925 she was examined at the Mayo Clinic. Dr. H. W. Woltman supplied the following clinical observations:

"A notation of the history of tremor in the family was made but, unfortunately was not amplified. For six years prior to examination in August

From the Department of Anatomy, Cornell University.

1925 the patient had displayed some eroticism; there was also evidence of mental deterioration, and she had lost her social finesse; whereas she had been prudish formerly, she had become almost vulgar at times, told people how to do things and was loquacious and at times befuddled. In August 1925 there was slight diminution in her ability to recognize methyl salicylate (oil of wintergreen), but she recognized camphor promptly on both sides. The right eye did not turn in on convergence, which may well have been due to failure of vision on this side. The pupil did not respond to direct illumination on the right but reacted to crossed illumination. There was atrophy of the right optic nerve, and the left disk was pale. A fine tremor was present in both upper extremities. This was also noticeable in the handwriting, which was otherwise good. Superficial and deep sensibility and stereognosis were normal. The weight was 170 pounds (77.1 Kg.) and the height about 5 feet and 4 inches (16 cm.). She was distinctly obese, and there was slight hypertrichosis of the face. There was distinct witzelsucht, and cooperation was limited. Vision in the left eye was 6/5, and there was temporal hemianopia for colors on the left; the right eye was blind. The systolic blood pressure was 154 mm. and the diastolic 84 mm. The sella was normal in size; the posterior clinoid processes suggested erosion and a calcified area measuring 4 by 2 cm. was present just anterior to the sella.

"The patient was reexamined on June 28, 1926, in the neurologic department. There was marked weakness of the lower extremities; rapid movement and static tremor of small amplitude were present in both upper extremities. There was slight dysarthria."

The epileptic attacks increased in severity, and they were now ushered in by a distinct olfactory aura resembling that of uncinate fits. Gustatory hallucinations were not mentioned. The patient's own description, given four years prior to her death, follows: "The attacks come on every seven to ten days. I used to lose consciousness without warning. I have had a premonition of the attack by having a peculiar odor come to me. It was like acid on iron. It was as if I poured vinegar into a hot skillet. As I think of it now, I have noted that same smell when making candy in years past, prior to 1920, before the epilepsy set in. I lose consciousness and fall when standing. I sometimes have convulsive movements of the face and hands. Every time, I bite my lips and the inside of my cheeks. At times I have two or three attacks a day, but usually only one. Then I feel reasonably sure I will be free from an attack for seven days or more. I do not feel very sick, except directly after an attack, but lack confidence in my ability to do any housework except mending or writing letters. On advice, I have taken bromides and phenobarbital, but I did not notice that they had any effect either to lessen or to prevent the attacks. Lately there have been no warning of odor, and I feel so sick I ask the family if I have had an attack (which has occurred without my knowledge)."

Her son confirmed her statements, adding other details. Early in 1933, the left breast was removed on account of a cancerous growth.[1] Throughout life her emotional responses were not affected and seemed to be normal almost to the end, when on occasions she lost her temper with her housekeeper. She slept much, but there was no abnormal somnolence. During the epileptic attacks of recent years, she sometimes lost control of the bladder and bowels. Bladder control seemed to be poorest. Muscular weakness increased, and there was some loss of general muscular con-

1. Footnote deleted.

trol. During the attack she salivated, but not at other times. The heart rate and most other autonomic functions were not noticeably affected. Occasionally she was disoriented in time, with lapse of memory, but not noticeably in space. Sometimes simple things were not clear, and frequently she insisted that things she had dreamed were true. Most of the time her mind was clear. Owing to wasting of the extremities, excess fat was largely, if not entirely, concentrated in the abdominal region, so that she looked like a woman in the last stage of pregnancy. She died of pneumonia.

Autopsy.—The brain, with the base of the skull enclosing the tumor of the optic nerve, was removed and sent to our laboratory at Ithaca, with other organs. The report was: The gallbladder was small and fibrotic and contained two stones about the size of a marble; the cavity of the gallbladder was filled with thick pus. The adrenal glands were enlarged bilaterally and measured about 3 by 2 by ½ inches (7.5 by 5 by 1.5 cm.). The uterus was small and atrophied.

Summary of Observations: The diagnosis was: a large meningioma of the right optic nerve, about the size of a walnut, embedded in the right anterior perforated substance of the brain; hypostatic pneumonia; cholelithiasis with suppuration, and bilateral tumor of the adrenal glands.

The cause of death was pneumonia; contributory causes were meningioma of the optic nerve (tumor of the brain) and adrenal tumors.

The meningioma infiltrated the right optic nerve and compressed the right olfactory region in front of the optic chiasm. The tumor was sectioned and classified by Dr. B. F. Hauenstein of the Ithaca Memorial Hospital.

Four lesions will be considered: (1) the meningioma of the right optic nerve sheath, compressing the olfactory centers; (2) atrophy of the right optic nerve; (3) dural calcifications and degeneration of thalamocortical fibers, and (4) lacunar softening of the left dorsal thalamus.

Meningioma of the Right Optic Nerve: Gross Observations: A round tumor, about 3 cm. in diameter, attached to the right optic nerve, was lodged in the posteromedial part of the right anterior cranial fossa and embedded in the corresponding orbital surface of the brain, compressing the olfactory tubercle and the anterior perforated substance.

The tumor was distinctly outlined and did not infiltrate the brain substance. When it was removed, the depression it produced in the brain measured 2.1 cm. in depth, 3.5 cm. in width and 3 cm. in the anteroposterior direction. Compression of this region was responsible for the appearance of the olfactory aura, the severe convulsive seizures and, possibly, the loss of bladder control.

The regions of the olfactory tubercle, olfactory trigon and anterior perforated substance (the sublenticular region) were compressed and practically obliterated by the tumor. The medial part of the parolfactory area of Broca was compressed into a thin sheet. The septum pellucidum was spared. The diagonal band of Broca was pushed back and partially obliterated. The posterior ends of the gyrus rectus and the rostral and suprarostral gyri were compressed. At the side of the tumor the orbital operculum was displaced laterally.

The right optic nerve and the tract in the region of the chiasm were invaded by the tumor and apparently were its site of origin. This was probably the original site of the lesion causing atrophy of the optic nerve and blindness. The temporal part of the left optic nerve was spared.

The right internal carotid artery was partially involved in the posterior side of the tumor. It was partially occluded just before it divides into the anterior and

the middle cerebral artery. Proximal to this occlusion was prominent distention of the artery. The lenticulostriate arteries were compressed by the tumor where they enter the anterior perforated substance. Other vascular distentions occurred in the neighboring regions of the brain.

The lateral ventricles were slightly distended. The septum pellucidum was displaced to the left. The corpus callosum was of normal size. The posterior displacement of the right amygdaloid and pyriform areas was so slight that it did not seem important.

Histologic Observations: The cortex was photographed from all sides. The hemispheres were removed by a circular incision around the insula and the corpus

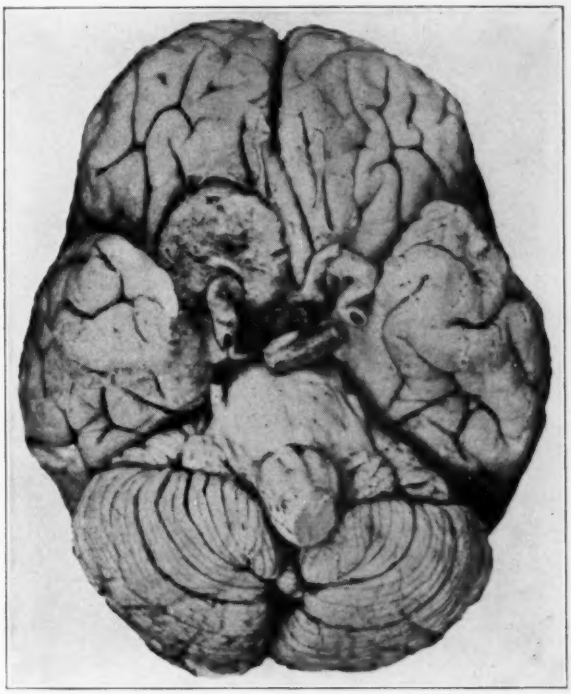

Fig. 1.—Basal surface of the brain, showing location of the meningioma.

striatum. Part of the midbrain, the thalamus and the corpora striata, including the insular regions and the site of the tumor, were trimmed to form one block. This was mordanted in a solution of potassium bichromate, embedded in pyroxylin and cut and stained by Mr. R. Wayne Rundles. Each tenth section was stained by the Weigert-Pal method. A cell stain was not successful. Owing to poor staining of the corona radiata, the fiber degenerations between the cortex and the internal capsule were not traceable.

The meningioma of the optic nerve compressing the basal olfactory centers on the right side (fig. 1) was the most prominent lesion and was responsible for the following abnormal conditions:

The olfactory tubercle and the anterior perforated substance were practically destroyed by compression. The lateral olfactory tract was completely lost. The

medial bundle of the forebrain on the right side was disrupted and degenerated in its entire extent (fig. 2). Its course through the lateral hypothalamic region, in which it ended, was clearly shown.

The septal region was displaced to the left, and its most medial fiber components stained well. The diagonal band of Broca passed behind the tumor and into the septum. It stained weakly.

The fiber field in the region of the diagonal band in front of the optic tracts stained fairly well. This is the region of the nucleus basalis and the origin of the

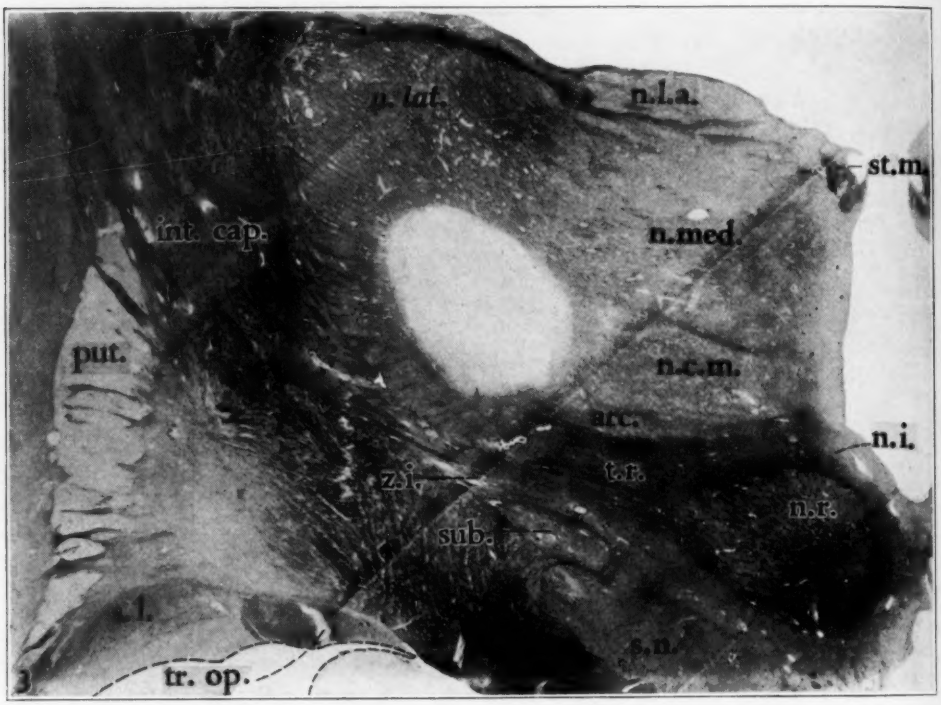

Fig. 2.—Section 240 of the brain. The large softened area in the ventrolateral nucleus of the thalamus is illustrated. In the figure *arc.* indicates the arcuate nucleus; *int. cap.*, the internal capsule; *n. c. m.*, the nucleus centrum medianum; *n. i.*, the interstitial nucleus; *n. lat.*, the nucleus lateralis; *n. l. a.*, the nucleus lateralis anterior; *n. med.*, the medial nucleus; *n. r.*, the red nucleus; *put.*, the putamen; *s. l.*, the sublenticular bundle; *s. n.*, the substantia nigra; *sub.*, the subthalamic nucleus; *st. m.*, the stria medullaris; *t. r.*, the tegmental radiations; *tr. op.*, the optic tract, and *z. i.*, the zona incerta.

right olfactohabenular tract, remnants of which passed across the degenerated medial bundle of the forebrain to enter the medullary stria of the thalamus.

The stria terminalis was normal on both sides. That on the right crossed through the degenerated medial bundle of the forebrain to end in the preoptic and supra-optic regions of the hypothalamus.

The right amygdaloid region did not appear to be affected (fig. 3). The anterior commissure was displaced but was normal except for the absence of the olfactory component on the right.

The hippocampi were small and possibly reduced in size. The fornix was partially demyelinated on the right and less affected on the left. The mamillary bodies and the mamillothalamic tracts were demyelinated, particularly on the right side.

The inferior thalamic peduncle on the right, posterior to the tumor, showed extensive demyelinization and loss of fibers (fig. 3). It appeared to come from the anterior, medial and ventromedial thalamic nuclei, passing ventrally and then laterally to end in the globus pallidus. The anterior thalamic radiation, which

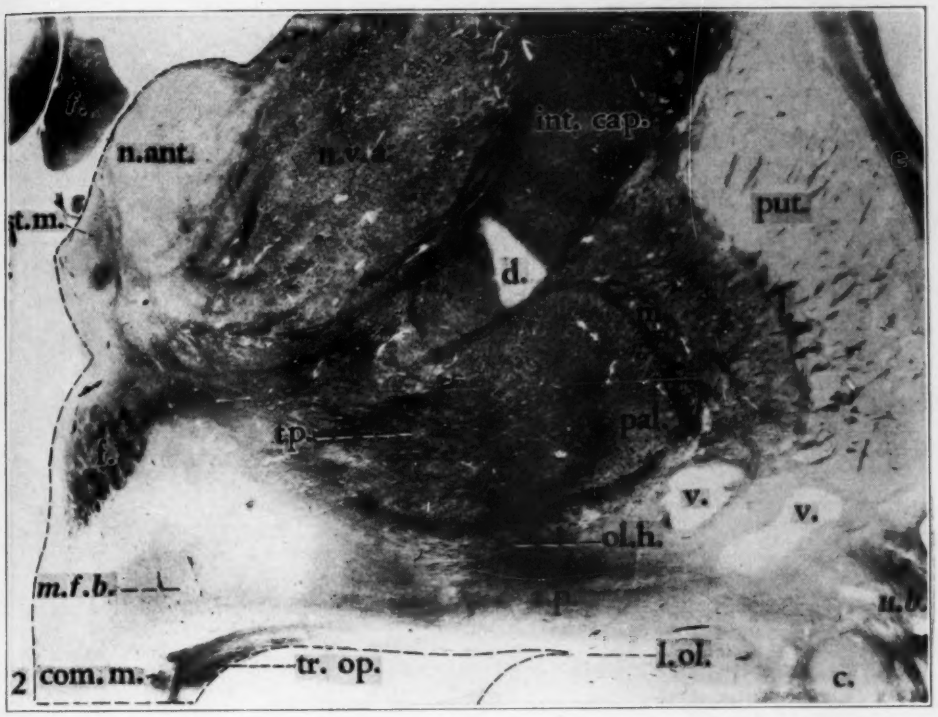

Fig. 3.—Section 430 of the brain. The degenerations in the internal capsule, optic tract, medial bundle of the forebrain and lateral olfactory tract are illustrated. In the figure *a. p.* indicates the anterior perforated substance; *c.*, the tail of the caudate nucleus, oral end; *com. m.*, Meynert's commissure; *d.*, the degenerated bundle in the internal capsule; *e.*, the external capsule; *f.*, the fornix; *int. cap.*, the internal capsule; *l.*, the lateral medullary lamina of the globus pallidus; *l. ol.*, the lateral olfactory tract (degenerated); *m.*, the medial medullary lamina of the globus pallidus; *m. f. b.*, the medial bundle of the forebrain (degenerated); *n. ant.*, the anterior nucleus of the thalamus; *n. v. a.*, the nucleus ventralis anterior; *ol. h.*, the olfactohabenular fibers; *pal.*, the globus pallidus; *put.*, the putamen; *st. m.*, the stria medullaris; *t. p.*, the thalamopallidal fibers; *tr. op.*, the optic tract; *u. b.*, the uncinate association bundle, and *v.*, vacuoles under the lentiform nucleus.

leads directly forward from these thalamic nuclei into the internal capsule, was slightly affected, as were the fibers which follow this course forward to arch ventrally through the internal capsule and enter the anterior portion of the pallidum. Both these thalamic peduncles were normal on the left side. The region of Forel's fields and the pallidotuberal fibers (Ganser's commissure) stained well on both sides.

In the ventral part of the right globus pallidus large, distended perivascular spaces surrounded some of the lenticulostriate vessels (fig. 3). Around these dilatations focal degenerations were apparent. Here, some of the fiber systems of the pallidum appeared to be stretched and displaced; some were apparently broken. On the right side there was weakening of the pallidomesencephalic fibers, which were followed downward over the red nucleus on that side. Otherwise, the large pallidorubral, pallidosubthalamic and pallidotegmental fiber systems stained normally. The strionigric fibers were not noticeably affected.

The anterior limb of the internal capsule was elevated and compressed on the right side, so that the frontopontile and cortical fibers descending to the substantia nigra showed considerable demyelinization. The left corticopontile tract was partially demyelinated.

The patient's motor weakness and difficulties were probably due in part to these degenerations.

Atrophy of the Optic Tracts: This lesion was present bilaterally (figs. 2 and 3), both tracts being severely degenerated. The left tract was the larger. Its homonomous temporal fibers were least affected. Its crossed fibers, from the right side of the chiasm, were completely degenerated. The right optic nerve, the right half of the chiasm and the adjacent part of the right optic tract were infiltrated by the meningioma. A part of the fibers crossing the chiasm from the left to the right optic tract retained their myelin. These deficiencies in myelinization were also evident in the lateral geniculate bodies, that on the right being much altered.

These lesions correlate with the blindness in the right eye and probably account for the patient's occasional groping for objects and disorientation in space. There was no record of visual hallucinations, but color blindness was present in the left temporal field. This suggests that color vision may depend on normal bilateral innervation of the lateral geniculate bodies.

The commissure of Meynert appeared to be preserved; on the right side it was fairly distinct, but on the left it stained weakly.

Dural Calcification.—There was a flat, nodular, bony plate in the dura close to the right side of the sagittal sinus and falx cerebri. This plaque compressed the cortex of the right paracentral lobule directly over the upper mesial end of the central sulcus. In this position it compressed the ends of both the precentral and the postcentral gyrus. The compression was restricted to the dorsal surface of the brain just at the dorsomesial margin of the right hemisphere. The cortex was depressed about 4 mm. The bony plate and depression measured about 1.5 cm. in the anteroposterior direction and about 1 cm. in the lateral direction. This compression, we think, caused degeneration of a band of corticothalamic fibers.

There were another very small bony plaque and compression of a similar nature about 3 cm. in front of the aforementioned lesion, situated in the right superior frontal gyrus. This compression may have been responsible for the poor bladder control. There was also a small bony nodule in the dura over the left hemisphere, situated about 2 cm. to the left of the midline and resting in the posterosuperior portion of the precentral sulcus.

The degeneration of the thalamocortical fibers probably was due to the lesion in the dorsomedial border of the motor area caused by the bony dural plaques. These fibers entered the upper middle portion of the internal capsule, from which point their course was readily followed (ventrad) into the thalamus. Above, this sclerotic band was situated over the external medullary lamina of the pallidum on the right side. Shifting medially into the internal capsule (fig. 3), it led down into the external medullary lamina of the thalamus and thence into the zona incerta, dorsal and lateral to the subthalamic nucleus of Luys. In this region there was a weakly staining area in the external part of the ventrolateral nucleus. Here the fibers appeared to end. Here, too, a number of distinct perivascular distentions occurred around small blood vessels in the external medullary lamina.

At this level, on the right side was another small degenerated fascicle of fibers leading upward into the internal capsule. It appeared to pass in the direction of the small frontal compression caused by the other dural plaque.

Lesion in the Left Thalamus.—This lesion, which may be described as lacunar or perivascular softening, occupied the central portion of the left ventrolateral nucleus of the thalamus (fig. 2). It was situated just lateral to the center median nucleus of Luys. The left thalamus was reduced in size. The center of the lesion was lacunar; the periphery was softened. Many degenerated fibers passed laterally into the internal capsule, but their course beyond was diffuse. As a result, the internal capsule on the left side was noticeably reduced in size and staining quality. However, a poorly stained and demyelinated stratum of fibers appeared in the left zona incerta. It seemed to pass through the internal capsule, to disappear in the left globus pallidus.

COMMENT

The position of the tumor was such as to press upward on the anterior limb of the right internal capsule and, to a lesser extent, across the midline, on the left capsule. This, with the vascular insufficiency, was probably the cause of the muscular weakness and atrophy of the frontal lobes. These, in turn, may explain the mental deterioration, lack of cooperation and witzelsucht.

The upper extent of the premotor cortex on both sides showed local atrophy. There was some atrophy of the mesial cortex of the right frontal lobe. The mental deterioration and witzelsucht may be attributed to this condition. The upper portion of the premotor area of the left cortex showed a localized region of atrophy, but the precentral and postcentral gyri were not affected. It is a question whether cortical atrophy on the left was not related to softening of the left ventrolateral nucleus of the thalamus.

The cortical compression on the right side and the cortical atrophy, more pronounced on the left, were located in the epileptogenic zone of Foerster and Penfield.[1a] The thalamic lesions were accessory factors in this case.

How much these degenerations had to do with the epilepsy is a question. The lesions in the olfactory centers probably account for the convulsive movements of the face and hands and the aura, and for the final

1a. Foerster, O., and Penfield, W.: The Structural Basis of Traumatic Epilepsy and Results of Radical Operation, A. Research Nerv. & Ment. Dis., Proc. **7**:569-591, 1931.

disappearance of the aura as the lesion attained an obliterating effect. Groff [2] found that epilepsy as a symptom of meningioma is more frequent than is generally supposed, occurring in about 30 per cent of cases. The tumors located in the olfactory region are recorded as giving rise to experiences of smell and convulsive movements of the face. As Lennox and Cobb [3] and others have pointed out, the convulsive state cannot be explained by focal lesions, which are to be regarded rather as predisposing causes. The statistics given by Parker [4] indicate that epileptic attacks are more frequently associated with tumors of the frontal lobe than with those situated elsewhere in the cranial cavity. The evidence presented by Bateman [5] shows that many pathologic conditions other than tumor may predispose to epilepsy. In the present case the cortical atrophy in the premotor area was in Bateman's field 1, which he found to be the most common site of cerebral shrinkage.

In view of the location of the meningioma in the basal olfactory region, it seems that in this case the quantitative olfactory tests of Elsberg [6] would have given localizing signs.

Since the mechanism of the convulsive seizures is still unknown, it is safe to say that the lesions and degenerations of the tracts described in this case have no certain bearing on any anatomic basis of epilepsy, which, per se, is a functional manifestation.

The adrenal tumors were probably the cause of the abdominal obesity. How the hypertrophy of the adrenals was related to the meningioma and to the tumor of the breast are unanswered questions.

SUMMARY

A case of epilepsy with olfactory aura is described in a physician who died at the age of 76. Twenty years prior to death there developed retrobulbar optic neuritis on the right, which resulted in blindness. An olfactory aura appeared, and five years later epileptic attacks began. A meningioma of the right optic nerve sheath which compressed the basal olfactory centers was observed at autopsy. A tumor of the breast had been removed surgically. The adrenal glands were greatly enlarged. Degenerations of various fiber tracts caused by the meningioma, dural calcifications and lacunar softenings in the left thalamus and elsewhere are described.

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4. Parker, H. L.: Epileptiform Convulsions: The Incidence of Attacks in Intracranial Tumors, Arch. Neurol. & Psychiat. **23**:1032-1041 (May) 1930.

5. Bateman, J. F.: Cerebral Frontal Agenesis in Association with Epilepsy, Arch. Neurol. & Psychiat. **36**:578-585 (Sept.) 1936.

6. Elsberg, C. A.: The Sense of Smell: The Value of Quantitative Olfactory Tests for the Localization of Supratentorial Tumors of the Brain, Arch. Neurol. & Psychiat. **36**:665-671 (Sept.) 1936.

Abstracts from Current Literature

Physiology and Biochemistry

Dietary Deficiency, Nerve Lesions and the Dental Tissues. J. D. King, J. Physiol. **88**:62, 1936.

In experiments on dogs and rabbits the effects of resection of certain nerves were compared with those due to vitamin A deficiency. In dogs receiving diets deficient in vitamin A, eruption of teeth was delayed; hypercementosis occurred, and the lamina dura and bone of the tooth sockets were malformed; the alinement of the incisor teeth was irregular, and there were additional periodontal and nerve defects. In animals in which the inferior dental nerve was resected on one side, the eruption in dogs and the growth of teeth in rabbits were accelerated; the alinement of the incisor teeth was irregular, but no defects in the dental or periodontal tissues were observed. As similar changes were observed on resection of the cervical portion of the sympathetic chain, the effects of severing the inferior dental nerve are regarded as due to damage to vasomotor fibers.

Alpers, Philadelphia.

Effects on the Knee Jerk of Stimulation of the Central End of the Vagus and of Various Changes in the Circulation and Respiration. A. Schweitzer and Samson Wright, J. Physiol. **88**:459, 1937.

In cats under anesthesia induced with a compound of chloral and dextrose (chloralose) the knee jerk was recorded from one leg, and the neuromyal response of the quadriceps muscle, from the other. The results of earlier investigators were confirmed in the demonstration of reflex inhibition of the knee jerk, with recruiting onset and prolonged after-discharge of the inhibitory effect following repetitive stimulation of the central end of either vagus nerve. The effect was independent of changes in circulation and respiration.

McCouch, Philadelphia.

Cevitamic Acid (Vitamin C) Content of Various Parts of the Central Nervous System and of Peripheral Nerves. I. Mělka, Arch. f. d. ges. Physiol. **237**:216, 1936.

Studies of the nervous system of rats, guinea-pigs, rabbits and calves and of the human brain gave the following results: The highest content of cevitamic acid in the human brain was observed in the pituitary gland and the cerebellum (average 0.26 mg. per gram). The cerebral cortex had an average of 0.17 mg.; the globus pallidus, 0.16 mg., and the medulla oblongata, spinal cord and white matter of the central nervous system, 0.13 mg., while peripheral nerves (sciatic nerve) have little cevitamic acid (averaged 0.03 mg.). In calves and rabbits the highest values were also in the cerebellar cortex. The cevitamic acid content of the brain depends to a high degree on nutrition; it dropped to below 4 per cent of the normal value if the food was free from cevitamic acid. At 18 C. (60.4 F.) the cevitamic acid content of the human brain does not decrease within twenty-four hours after death.

Spiegel, Philadelphia.

Experimental Changes of the Phylogenetic Relations of the Vagus Nerve. P. Anochin and A. Iwanow, Arch. f. d. ges. Physiol. **237**:536, 1936.

An anastomosis was produced in dogs between the central stump of the vagus nerve and the distal part of the brachial plexus, and the phenomena of gradual "reintegration" were studied. After from one to four months stroking the skin on the external and internal surfaces of the foreleg elicited coughing, and

eventually vomiting. At this stage the vagus nucleus still had its specific reaction to afferent stimuli; it also reacted only to special stimuli, such as stroking the skin or stretching the muscles, while a pin-prick elicited typical pain reactions. During the subsequent months the type of reaction changed; it became more difficult to elicit the visceral reactions (coughing and vomiting) by stroking the skin, while a local reaction of the foreleg appeared. Thus, the response of the vagus nucleus changed from a predominantly visceral to a predominantly somatic reaction. The paralyzed muscles of the foreleg reached their maximum atrophy from three to four months after operation. After from four to six months stimulation of the vagus nerve above the anastomosis yielded flexion or extension of the leg; stimulation of the motor cortex also resulted in movements of the foreleg on the side of operation. The experiments seem to indicate that reintegration in the central nervous system is initiated by impulses from the periphery and is under their constant control.

SPIEGEL, Philadelphia.

CONSTANT DIFFERENCES IN THE ACTION POTENTIAL PATTERN OF HUMAN MUSCLES IN VOLUNTARY INNERVATION. O. F. VON SCHWERIN, Deutsche Ztschr. f. Nervenh. **142**:18, 1937.

The action potentials of the flexor muscles showed a considerably lower frequency than those of the extensor muscles in voluntary innervation against slight resistance. These findings were constant in eleven normal subjects and in four patients with nervous disease, three of whom had spastic symptoms and the fourth cerebellar ataxia. It is noteworthy that the difference between the extensor and the flexor muscles was seen also in the spastic limbs. The results seem to be in contrast to the findings of Bourguignon, who stated that the chronaxia of the extensor muscles is normally twice as long as that of the flexor muscles and becomes equal in spasticity. The author points out that the length of the fibers may play a part, in that the frequency of the action potentials is higher in the muscles with the shorter fibers. A hypothetic explanation given by the author is that the muscles with short fibers have more numerous nerve fibers and thus receive more frequent impulses.

HOEFER, Boston.

Neuropathology

ACTINOMYCOTIC ABSCESS OF THE BRAIN. HOWARD ZEITLIN and BEN W. LICHTENSTEIN, Arch. Path. **23**:58 (Jan.) 1937.

Actinomycosis of the central nervous system is rare and usually occurs as a hematogenous metastatic lesion from a focus elsewhere in the body or as the result of direct extension from lesions involving the skull and soft parts of the face and throat. More rarely, it represents primary involvement of the nervous system.

The clinical picture in the case reported resembled that of tuberculous meningitis, but the changes in the spinal fluid suggested purulent meningitis secondary to pulmonary involvement. Autopsy revealed the following conditions: two actinomycotic abscesses of the right frontal lobe, with perforation of one into the lateral ventricle; diffuse suppurative leptomeningitis and a small cavity with actinomycotic filaments in the lower lobe of the left lung.

Although a number of cases of primary actinomycosis of the central nervous system have been reported in the literature (twenty-three cases were mentioned by Friedman, Plaut and Levy), further examination revealed that the necropsy records were incomplete and inadequate in most instances. This was due to inadequate postmortem examination of the middle ears, paranasal sinuses, tonsils and other organs which might originally have harbored the organisms.

The possibility of failure to identify the primary source of infection at necropsy is illustrated in the case reported. The observation of Actinomyces in the abscesses of the brain led to immediate search for a possible primary source of infection. Examination of the throat, sinuses and middle ears and reexamination of the lungs and abdominal organs failed to disclose an active actinomycotic lesion at the time.

Thus, at first the possibility of primary actinomycotic abscess of the brain was considered. Additional history obtained from the family revealed that the patient had sustained a trauma to the head two months prior to onset of the symptoms. It was only after fixation of the lungs in Kaiserling's solution that careful sectioning into very thin slices disclosed a primary focus of infection in the form of a small, circumscribed cavity in the lower lobe of the left lung.

According to Jacoby, actinomycosis may involve the central nervous system in the form of meningitis, an encapsulated abscess or a gelatinous granulation tumor. The meningeal type, in which infection usually takes place by continuity, is the most frequent. The lesion erodes all structures in its path. Localized abscess of the brain usually has a hematogenous source in the lungs, mouth or gastro-intestinal tract. Invasion along the lymphatics and lymph glands, except for the perineurial spaces in the nervous system, has not been noted.

WINKELMAN, Philadelphia.

CEREBRAL LESIONS IN HYPOGLYCEMIA. A. B. BAKER and N. H. LUFKIN, Arch. Path. **23**:190 (Feb.) 1937.

This paper gives in detail the histologic changes in the brain in three cases of hypoglycemia. Review of the literature revealed that no consistent lesions have been reported. Some authors describe normal conditions of the brain, and some, extensive changes in the cells, fibers and blood vessels. The most common condition reported was a change in the ganglion cells. Experimental studies on animals also gave evidence of extensive damage to the ganglion cells, which was more severe in cases in which convulsions occurred. Investigators also reported petechial hemorrhages throughout the cerebral hemispheres.

Detailed histologic studies of the central nervous system in the three cases of hypoglycemia reported by Baker and Lufkin revealed certain features that warrant emphasis. There were extensive and widespread alterations of the ganglion cells, involving both the cytoplasm and the nucleus. The degree of destruction varied in each section and in each case studied. There apparently was no localization in any layer of nerve cells, or even in any part of the brain; the injury was usually disseminated. Cellular changes similar to these are observed in normal brains. The character of the changes strongly suggested postmortem alteration; therefore, in spite of the fact that other authors have described cellular alterations in the brains of persons with hypoglycemia, Baker and Lufkin hesitate to ascribe too much significance to the observations in their cases.

There remained the possibility, however, that some antemortem damage to the cells had occurred and was masked by the changes resulting after death. In order to verify this point, experiments on animals were undertaken, in an attempt to obtain absolutely fresh nerve tissue. It was readily apparent from these experiments that the cellular alterations, even those observed after many severe hypoglycemic attacks, are negligible. The ganglion cells were normal in size, shape and structure and failed to reveal the extensive changes seen in the human material. This observation seemed to strengthen the original impression that the cell changes which were observed in man probably had occurred post mortem and were of no significance.

A final feature of the study was the presence of tiny hemorrhages scattered irregularly throughout the brain. In most sections the size and distribution of the petechiae were of such a nature that no apparent injury was done to the surrounding tissue, the erythrocytes merely pushing the cerebral fibers apart, without causing destruction. Little or no alteration in the normal cerebral function would be expected to occur as a result of these tiny petechiae. However, there remained the likelihood that during a severe convulsive seizure the resulting hemorrhages might become confluent, with resultant injury to the surrounding brain tissue by pressure or destruction. Such a process occurring within an important brain center could well give rise to temporary or permanent neurologic manifestations, long after the restoration of the rest of the brain to normal function.

WINKELMAN, Philadelphia.

AN UNUSUAL ANATOMICOCLINICAL COMBINATION OF LETHARGIC ENCEPHALITIS AND DISSEMINATED SCLEROSIS. A. DE WULF and L. VAN BOGAERT, Ann. de méd. **39**:417 (April) 1936.

Though Guillain and Alajouanine (1927) denied a direct relationship between lethargic encephalitis and disseminated sclerosis, isolated instances of the simultaneous occurrence of these diseases have been observed from time to time. They tend to show that the virus of lethargic encephalitis may produce areas of demyelinization and glial proliferation. In the present case lethargic encephalitis at the age of 13 years was followed by severe changes in personality. Five years later mild tremor of the whole body developed and was followed gradually by increasing spasticity of the extremities and severe salivation. The clinical picture differed, however, from that of postencephalitic parkinsonism in the presence of bilateral lesions of the pyramidal tract and intense dysarthria. Death occurred at the age of 27. The anatomic diagnosis was disseminated sclerosis with marked periventricular demyelinization. Histologically, besides the characteristic multiple plaques of different ages disseminated throughout the whole central nervous system, there was extreme atrophy of the substantia nigra bilaterally, with degeneration of the pigmented cells and abundant glial proliferation, similar to the histologic changes in postencephalitic parkinsonism. De Wulf and van Bogaert conclude that in this case two pathologic processes were superimposed one on the other—postencephalitic parkinsonism and disseminated sclerosis. "Nothing permits one, however, to conclude that the encephalitis virus produces isolated foci of demyelinization which might be compared to the plaques of disseminated sclerosis."

WEIL, Chicago.

HISTOGENESIS OF NEOPLASM OF THE HYPOPHYSIS. C. JAKOB, Rev. neurol. de Buenos Aires **1**:99 (Sept.) 1936.

There are two types of cellular elements in the different parts of the hypophysis: the young reserve elements, or histioblasts, and the mature active elements, or histiocytes. Neoplasms may develop from either type, forming hypophysioblastoma and hypophysiocytoma. This differentiation is not always absolute, since there exist combined forms. This division has its clinical importance, since only the hypophysiocytoma is accompanied by endocrine symptoms.

From the normal histiocytes there may develop eosinophilic adenoma and adenocarcinoma with and without acromegaloid symptoms, basophilic adenomatous tumor with and without alterations in metabolism and, finally, mixed forms. From the ectodermal histioblasts there may develop adenoblastoma without endocrine symptoms. The mesenchymal elements give rise to endothelioma, fibroma, angioma and their sarcomatous derivations; rarely is there neuroma or neuroganglioma.

There are three possibilities in the growth of these prehypophysiomas. The most benign forms may only widen the sella turcica without leaving it, or they may invade the cranial base, compressing the nerves at the base (second, third, fourth and sixth cranial nerves); the malignant adenocarcinomatous forms invade the cerebrum, compressing the peduncles and the ganglia of the base. A third malignant group, especially the sarcomatous and angiomatous forms, invades below the cranial osseous base and penetrates the retronasal space.

From the dorsal rudimentary peri-infundibular portion, of ectodermal origin, analogous in its structure to the anterior lobe, there develops hypophysioblastoma without endocrine phenomena; the tumor grows rapidly and has a tendency to secondary regressive phenomena (necrosis and hemorrhage).

From the glandular intermediate portion formed by the colloid tubes and interstitial tissue, there may grow typical primitive struma, with colloid secretion, comparable to that of thyroid origin.

ALPERS, Philadelphia.

ANATOMIC AND HISTOLOGIC STUDIES IN CASES OF SCHIZOPHRENIA. F. MEYER, Monatschr. f. Psychiat. u. Neurol. **91**:185 (July) 1935.

This study is a continuation of the work reported in an earlier paper (*Monatschr. f. Psychiat. u. Neurol.* **88**:265 [May] 1934). Six additional cases were investigated by Meyer. In general, the results were similar to those already reported. However, in three cases the brain failed to show noteworthy parenchymal changes. The atrophic, infiltrative and productive lesions previously observed in the gastro-intestinal tract were lacking in two cases. Collections of cocci were observed in the brain in one case and in the liver, spleen and adrenal glands in another. The splenic lymph follicles exhibited foci of necrosis in one case. An increase of connective tissue was frequently noted in the thyroid, adrenal and pituitary glands, but accumulations of round cells were not observed. The intensity of the disturbances and their distribution bore no relation to the duration of the illness. Some of the alterations obviously pointed to a septic process, probably of terminal nature. The fact that the lesions discovered in the gastro-intestinal tract did not occur in all cases indicates that they cannot be brought into direct etiologic relationship with the mental disorder. It is possible that they are secondary to the disturbances in the endocrine system. The endocrine changes apparently represent a primary sclerotic process, which may have occurred in reaction to exogenous influences. Meyer believes that they are not primary causative factors but merely one component of the total picture of schizophrenia, the actual etiology of which is still obscure.

ROTHSCHILD, Foxborough, Mass.

CEREBRAL CHANGES IN DELAYED DEATH AFTER HANGING AND LIGATION OF THE CAROTID ARTERY. G. DÖRING, Virchows Arch. f. path. Anat. **296**:666, 1936.

Many of the changes that occur in the brain have been ascribed by Spielmeyer and his followers to circulatory disturbances. In such cases the circulatory alteration has been of more or less prolonged duration. When cessation of the cerebral circulation leads immediately to death, few changes other than capillary hemorrhages are observed. Döring describes the early histologic changes in two cases. Death occurred in one instance ninety-six hours after an attempt at suicide by hanging and in the other fifty-eight hours after ligation of the right common carotid artery. In each case there were multiple necroses of the cerebral cortex with no characteristic localization. The necrosis of the basal ganglia was of the coagulation type. The globus pallidus was severely damaged; in the case of death due to hanging this change was bilateral, and in the other case it was limited to the side of ligation. The ganglion cells revealed acute degenerative changes of varying degrees, and the glia, only early regressive changes.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

TUMOR OF THE PINEAL BODY. E. BENEKE, Virchows Arch. f. path. Anat. **297**:26, 1936.

A boy aged 16 had complained for several years of headache, polydipsia and polyuria. The body size and configuration were normal for the age. The penis was of normal size. The testes appeared to be atrophic. Death occurred in coma, with convulsive contractions of the extremities, rapidly rising temperature and respiratory paralysis. Necropsy revealed a midline tumor of the pineal region, with the dimensions of 3.2 by 4 cm. on the cut surface. The tumor had filled the third ventricle. Except in an area where the tumor had invaded the brain, it was sharply delimited and encapsulated. The neoplasm was a teratoma with derivatives of the three germ layers. It probably originated from pluripotent cells of the primitive streak. The invasive part of the tumor consisted of pineal tissue with an indistinct alveolar arrangement. The seminal tubules of the testes were hypoplastic, but the interstitial tissue was hyperplastic. In this case the macrogenitosomia that has been associated with pineal tumors was not evident.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

LEAD GANGRENE AND ENCEPHALOPATHY. E. RUTISHAUSE, Virchows Arch. f. path. Anat. **297**:119, 1936.

A man aged 68 years had had difficulty in walking and repeated attacks of intermittent claudication nine years prior to death. Gangrene of both lower extremities required four amputations in the course of the next three years. Histologic examination of the vessels of the amputated tissues revealed no arterial changes to account for the thrombosis, and emoblism was excluded. At the time of the first admission mild diabetes was detected. Death occurred, with symptoms of chronic nephritis and progressive paralysis. Necropsy revealed marked, extensive arteriosclerosis with calcification and ossification, malignant nephrosclerosis and a fragment of a lead projectile weighing 2.5 Gm. in the left occipital region of the brain. Later questioning brought to light a gunshot injury about thirty-nine years prior to death. Quantitative chemical examination of the various organs, including the brain, showed the presence of large amounts of lead. Histologic examination of the brain yielded no evidence of syphilitic dementia paralytica but rather such changes as have been described in some cases of lead encephalopathy. Rutishauser's interesting interpretation is as follows: Chronic lead poisoning led to injury of the pancreas and mild diabetes. The gangrene of the lower extremities, without evidence of arteriosclerosis at that time, was the result of more manifest lead poisoning with vascular spasm. The onset of more active symptoms of lead poisoning after a latent period of thirty-nine years was due to mobilization of lead through the acidosis of the diabetic state. Continuing and progressive lead intoxication caused arteriosclerosis, nephritis and the degenerative cerebral changes of lead encephalopathy.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

CLINICAL AND PATHOLOGIC STUDIES OF THE DIENCEPHALON. YUSHI UCHIMURA, Psychiat. et neurol. jap. **40**:55 (Oct.) 1936.

The diencephalon was investigated in the following diseases: paralysis agitans, pellagra, chronic morphine poisoning, cerebral arteriosclerosis, cerebral softening, meningitis of various types, parkinsonism, encephalitis B, dementia paralytica, Wernicke's polio-encephalitis and tumor of the brain. Special attention is called to the endarteritic changes in the mamillary bodies in the brain with dementia paralytica. These are similar to the endarteritis of Wernicke's polio-encephalitis but differ in that they are confined to the mamillary bodies. These changes occurred in five of twenty-eight cases, and in these instances there were symptoms common to one another, such as disturbance of consciousness, delirium and hallucinations. Further attention is called to the occurrence of true Wernicke's polio-encephalitis in the brain in postoperative psychoses.

ALPERS, Philadelphia.

LEUKEMIA AND THE CENTRAL NERVOUS SYSTEM. R. GORDIN, Acta psychiat. et neurol. **11**:227, 1936.

Changes in the nervous system are frequent in leukemia. Focal nervous symptoms are usually caused by hemorrhages in the brain and meninges, with resulting hemiplegia or epileptic fits. The hemorrhages are, however, nonspecific in leukemic involvement of the nervous system. Infiltration of the nervous system with lymphoblastic tissue is less common. This may involve the brain, cerebral meninges and cranial nerves, the spinal cord with its meninges and spinal nerve roots and the peripheral nerves. Intracerebral lesions consist chiefly of perivascular round cell infiltrations in the hemispheres, pons and medulla, with resulting circulatory disturbances and multiple small foci of softening. Involvement of the meninges is usually combined with that of the cranial nerves. The facial nerve is most frequently affected. The lesion consists usually of hemorrhages in and leukemic infiltration of the perineurium, with resulting degeneration of the nerve fibers. Leukemic tumors within the vertebral canal are the most common lesions of the spinal cord in this disease. Usually there are epidural lymphoblastomatous infiltrations. The infiltrating tissue compresses the cord and nerve

roots and penetrates into the intervertebral foramina. In some instances the leukemic infiltration spreads into the perivertebral tissues. Involvement of the peripheral nerves is rare. In addition to lymphomatous infiltration and compression of the spinal cord, there occur in the cord nonspecific secondary changes, viz., combined funicular degeneration due to anemia. Gordin reports a case of acute lymphatic leukemia which showed clinical symptoms of rapidly progressive ascending spinal paralysis with eventual development of myelomalacia of compression of the spinal cord by an epidural lymphoma at the level of from the third to the seventh dorsal vertebra.

YAKOVLEV, Waltham, Mass.

Psychiatry and Psychopathology

FUNCTIONAL PSYCHOSES IN CHILDREN. LOUIS LURIE, ESTHER TIETZ and JACK HERTZMAN, Am. J. Psychiat. **92**:1169 (March) 1936.

In a review of one thousand problem children studied at the Cincinnati Guidance Home, the authors found that twenty were psychotic. This proportion (2 per cent) suggests that mental disease is more frequent in children than has commonly been supposed. The ages of the twenty psychotic children ranged from 5 to 17 years; thirteen showed schizophrenia; one psychosis with encephalitis and six psychoses with psychopathic personality. In most of the schizophrenic group the onset was acute, whereas in all cases of psychopathic personality the development of the psychosis was insidious. In most of the children with dementia praecox intellectual impairment, taking the form of poor school work, was noted early in the illness, but actually the alteration in intelligence was not great as determined by psychometric tests. Development of antisocial trends or socially unacceptable behavior occurred at the beginning of the psychosis in most of the subjects. Eight of the thirteen schizophrenic patients came from good homes, whereas all the children with psychopathic personality had bad social backgrounds. Broken homes, for example, occurred in five of six cases of psychopathic personality and in only four of the thirteen cases of schizophrenia. The cases were reviewed many years later (on an average, six years after diagnosis); nine of the patients were in a hospital for mental diseases; three were doing fairly well in the community and three badly; one was in prison and one in a colony for the feebleminded, and three were not located. The authors believe that, in the absence of organic disease or mental deficiency, a child who shows simultaneously a break in the normal progress of his intellectual, emotional and social development is likely to have a psychosis later in life.

DAVIDSON, Newark, N. J.

ANXIETY SYNDROME: EVERYDAY PROBLEM OF GENERAL MEDICINE FREQUENTLY CONFUSED WITH HYPERTHYROIDISM. E. G. BILLINGS, Colorado Med. **34**:14 (Jan.) 1937.

Billings asserts that during the last two years one of every twenty-one adults newly admitted to the Colorado General Hospital and Dispensary was referred to the psychiatrist for diagnosis and treatment. In at least 45.5 per cent of cases the so-called functional conditions were incorrectly diagnosed and unsuccessfully treated as hyperthyroidism. The anxiety syndrome occurs in a person who is tense and uneasy and is characterized by rather suddenly occurring, transient attacks lasting from a few seconds to an hour, during which the patient subjectively experiences difficulty in breathing, palpitation, precordial discomfort, perspiration or "cold sweats," vertigo, various complaints referable to the gastrointestinal tract and a feeling of weakness. With these attacks there is invariably existent an underlying and accompanying emotional factor which is best described by the term "anxiety." If the physician elicits the complete complaint, he will usually learn that the patient has difficulty in sleeping, has some anorexia, tires easily, has a "tight" pain in the head, feels slowed up or confused in his thinking, is irritable and restless, has lost weight, has not been up to par for some time, "feels worried" without knowing about what or why and almost always feels cold

and "cannot get warm enough." The first step in therapy is elicitation of the complete complaint of the patient. Any situational factors dominant in the production of the illness must be altered if possible, or, if impossible, the patient, through discussions, should be led either to accept the facts as they exist or to modify his attitude toward them. Practically never is one situation or one factor the whole cause of the illness. Any medication given such a patient should be accompanied by a careful and painstaking explanation that the particular medication is only a means of giving symptomatic relief. In the young and middle-aged, barbital in doses of 1 grain (0.065 Gm.) morning and noon, and perhaps 2 grains (0.13 Gm.) at bedtime, will relieve the patient of considerable tension and uneasiness and thus promote clearer thinking, make less likely the occurrence of an anxiety attack, relieve the sensations in the head and allow for more adequate rest and sleep. In elderly patients sandoptal (isobutylallyl barbituric acid) seems to be better tolerated. When gastro-intestinal symptoms exist, 10 drops of tincture of belladonna three times daily, liquid petrolatum and a full diet with some roughage have proved helpful. If the gastro-intestinal symptoms are due more to an atonic condition of the intestine, gynergen in doses of 1 mg., twice daily for a few days, often gives relief. In case of a profound and prolonged anxiety attack with a tendency of the patient to become panicky, acetylcholine bromide in a dose of 1½ grains (0.1 Gm.), given intramuscularly, may aid in ameliorating the attack and thus save the patient from panic. EDITOR'S ABSTRACT. [J.A.M.A.]

ROLE OF SYPHILIS OF THE NERVOUS SYSTEM IN THE PRODUCTION OF MENTAL DISEASE: SURVEY OF VARIOUS FORMS OF NEUROSYPHILIS OCCURRING AT THE BOSTON PSYCHOPATHIC HOSPITAL FROM 1912 TO 1934. MERRILL MOORE and H. HOUSTON MERRITT, J. A. M. A. **107**:1292 (Oct. 17) 1936.

Moore and Merritt state that syphilis of the central nervous system was considered as the cause of mental disease in 2,468 patients admitted to the Boston Psychopathic Hospital in the first twenty-two years of its existence—from 1912 to 1934. When corrections were made in the total number of admissions for the proportion of patients who were found to be "not psychotic" and for the number of readmissions, syphilis of the nervous system was considered the cause of mental disease in 9.3 per cent of the total. Dementia paralytica and the tabetic form of dementia paralytica constituted 94 per cent of the 2,468 cases of mental disease due to syphilis of the central nervous system. EDITOR'S ABSTRACT.

A SURVEY OF THE EXTENT AND NATURE OF OFFENSES COMMITTED BY DELINQUENT BOYS. MERVIN A. DUREA, J. Juvenile Research **19**:62 (April) 1935.

As a basis for the study, reasonably detailed histories were procured of 368 boys confined in an institution for juvenile delinquents. All were white. A total of 1,148 offenses had been committed by the 368 boys. Multiple offenders were frequent; 31 per cent of the boys had committed 3 offenses. The offenses consisted of truancy, in 14 per cent; incorrigibility, in 20.8 per cent; stealing, in 25.3 per cent, and burglary, in 17.8 per cent. Thus, four offenses accounted for 77.9 per cent of the total number. The proportion of offenses involving acquisitive behavior to those involving nonacquisitive delinquency was 631 : 400. Offenses against property, violation of social demands or social decency and offenses against persons occurred in the relationship of 680, 436 and 32, respectively. There is an inverse relationship between offenses ranked as to seriousness in terms of differential weightings and those ranked as to seriousness on the basis of frequency of occurrence. Subjects whose first offense is truancy tend as a group to be younger than those whose initial offense is incorrigibility, stealing, larceny or burglary. The median life age is oldest for subjects whose first offense is larceny. Incorrigible boys who are first offenders tend as a group to be younger than those whose first offense is larceny; similarly, subjects whose initial offense is stealing tend to be younger than those whose first offense is larceny.

FERGUSON, Niagara Falls, N. Y.

THE DYNAMICS OF GROUP PSYCHOTHERAPY AND ITS APPLICATION. LOUIS WENDER, J. Nerv. & Ment. Dis. **84**:54 (July) 1936.

This article undertakes an analysis of the methods and results of treatment of patients in groups, during a period of six years. Of seventy-five patients treated with group psychotherapy, it was found that many were suitable for intramural treatment when psychoanalysis in the orthodox sense was impractical. The basis of therapy is the consciousness on the part of the patient that he is one of a kind, and this identification of himself with the group enables him to form useful transference to other members of the group and indirectly to the physician in charge. Group psychotherapy is applicable only to disorders in which intellectual impairment is absent and some degree of affect is retained. Early schizophrenia in which the delusional trends are not fully systematized, depressions without marked retardation and the psychoneuroses, exclusive of severe compulsion neuroses, are considered suitable for this treatment, but the method does not preclude the continuance of individual treatment.

A group consists of from six to eight persons of the same sex treated in two or three sessions a week of one hour each, for from four to five months. New patients are not admitted to a group already in session. The patients in a group are instructed not to discuss the content of the session with patients outside the group but are encouraged to discuss the material freely with one another. Sessions are devoted to single expositions of why a person behaves as he does, primitive instinctive drives, conscious and unconscious elements, the significance of dreams, early infantile traumas, reaction formations, repressions and rationalizations.

A sense of intimacy develops within the group, with greater freedom from inhibitions. When resistances are observed in any patient, careful guidance can divert the discussion into safe and still theoretical waters. A carefully gaged awareness as to the individual and collective reactions of the group is essential. In the group the patient learns criteria for evaluating his own problem against the problems of others in a way that is not feasible in individual treatment. Lessening of personal tensions occurs, and a desire to get well is given new impetus with the motive of a new ego ideal. The method cannot be evaluated statistically, but years afterward patients have attributed the capacity to discuss their problems freely and meet problems successfully to this group experience.

HART, New York.

THE SLEEP OF YOUNG CHILDREN IN A TWENTY-FOUR HOUR NURSERY SCHOOL. MARTHA REYNOLDS, Ment. Hyg. **19**:602 (Oct.) 1935.

A study of the sleep of nursery school children at the Vassar College summer school indicates that children between the ages of 2 and 3 years sleep approximately twelve hours and a half daily; those between the ages of 3 and 4 years, eleven and a half hours, and those between the ages of 4 and 5 years, eleven hours. Other factors, such as physical condition and emotional stability, probably affect the amount of sleep required. Reynolds asks whether the old standards were not too high and therefore the cause of anxiety and tension over the sleep problem. Children of all groups in the nursery school took approximately one hour instead of twenty minutes to go to sleep at night, and at nap time, half an hour.

It is suggested that specialists give serious consideration to the standards of sleep they urge parents to follow, since a revision of the attitude toward sleep similar to that of the attitude toward eating may be necessary in order to avoid the manufacture of sleep problems. Although the variations in the amount of sleep taken by individual children from day to day were large and inconsistent, the small variations in the weekly, biweekly and triweekly averages seem to indicate that, for a week or a longer period, there may be a tendency to maintain a fairly constant balance of sleep. Reynolds suggests that, instead of overemphasizing the importance of immediate external conditions, one should establish regularity of hours for rest, provide conditions conducive to sleep and arrange an adequately balanced day, free from emotional strain. If this is done, the physiologic demand for rest can be trusted to provide adequate and more or less automatic regulation.

DAVIDSON, Newark, N. J.

MENTAL DISEASES IN NEW YORK STATE ACCORDING TO NATIVITY AND PARENTAGE. BENJAMIN MALZBERG, Ment. Hyg. **19**:635 (Oct.) 1935.

The incidence of mental disease, measured by rates of first admissions of all white patients to institutions in New York State in three years, appears to be twice as high among the foreign-born as among the native-born. When populations are standardized on the basis of age and sex, however, the excess in the rate for the foreign-born is only about 19 per cent. Usually, the lowest rate is found among natives of native parentage; natives of foreign parentage have standardized rates intermediate between those for natives of native parentage and those of the foreign-born; the highest rates are found among natives of mixed parentage. In cerebral arteriosclerosis a high rate was found among native males of mixed parentage. In dementia paralytica the highest rates occurred in the mature decades of life and decreased at the older age levels. In alcoholic psychoses the rate for the foreign-born was reduced to a level below that for the second generation of foreign-born persons. In manic-depressive psychoses there were comparatively slight differences between the rates for the foreign-born and those for natives of mixed parentage. In dementia praecox the striking features were: the early maximum of cases in males between 20 and 30 years of age, with the maximum in females about ten years later; the higher rates for males through the thirties; the generally higher rates for females after the age of 40, and the significantly lower rates for natives of foreign and mixed parentage than for the foreign-born.

Although it is evident that the foreign-born have rates of mental disease in excess of those for persons of native birth, the excess is due largely to the effects of the age composition of the two populations. The rates apparently do not measure differences of a biologic order. Variations are due, probably, to social and other environmental influences, so that a complete determination of the relative difference in rates requires consideration of environmental and economic factors.

DAVIDSON, Newark, N. J.

AN INVESTIGATION OF DETERIORATION OF "GENERAL INTELLIGENCE" OR "G" IN PSYCHOTIC PATIENTS. M. R. HARBINSON, Brit. J. M. Psychol. **16**:146, 1936.

Thirty-six patients were given Terman vocabulary, or "V," tests and visual perceptual tests of general ability, or "G" tests. The vocabulary tests were considered to indicate the patient's intelligence before the illness (Babcock), and the visual perceptual tests, the intelligence at the time of testing. Hence, the difference in scores was a measure of deterioration during illness. Though the group of patients was too small for conclusive statistics, it is interesting that only 27 per cent of the eleven patients with schizophrenia showed deterioration, while 77 per cent of the thirteen patients with melancholia had apparently deteriorated. Of the ten patients falling into neither group, 40 per cent showed evidence of deterioration.

ALLEN, Philadelphia.

A CONTRIBUTION TO THE STUDY OF SCHIZOPHRENIA. R. LAFORGUE, Internat. J. Psycho-Analysis **17**:147 (April) 1936.

Laforgue describes the case of a young girl with schizophrenia, who had had symptoms of regression, mutism, withdrawn and bizarre behavior for several years. The patient was treated for several years, with socialization and good insight into her own condition but with inability to do without the help of the analyst.

The remarkable feature in the case is the long, tedious period of treatment during the phase of complete negativism and withdrawal. For a long time the analyst had to content himself with giving interpretations to the patient, without any evidence of response. The only way in which the effect of interpretation could be estimated was by watching the pulse, which occasionally rose to 130

when significant points were touched on. The acceleration of the pulse was occasioned chiefly by words connected with love and sexuality. The extreme sensitivity of the schizophrenic subject was again manifest in this patient. "The only thing to do was to handle words as carefully as if they were bombs and, as far as possible, soften their effect." Gradually, the patient began to respond verbally to the analyst and even explained some of her feelings.

The patient explained the loss of affect as follows: "To feel was to sin and so one must become unable to feel." When the patient decided to lose her feelings, she could not integrate her personality, as integration of personality is largely the correlation of various senses; this could not be accomplished, as any form of sensation is forbidden.

The general capacity for feeling is a special function exercised by the ego. The ego serves as an intermediary between the external and the internal realities, through coordination of the sensations in the outside world. This integration of sensations makes for knowledge and gives one an idea of what is going on around one. The patient began to improve when she recognized and admitted the right to have feelings and sensation, especially sexual feelings. This helped her to reconstruct the unity of her ego and thus arrive at a correct conception of reality.

KASANIN, Chicago.

SINUS SEPSIS AND MENTAL DISORDER. R. E. JOWETT, J. Ment. Sc. **82**:28 (Jan.) 1936.

Jowett reviews the work of Graves and his associates (*J. Ment. Sc.* **78**:459 [July] 1932), who demonstrated infection of the sinuses in 818 of 1,000 cases in which examination was made by exploration suction technic. Over 50 per cent of the patients have subsequently been discharged from the hospital for mental diseases, presumably after appropriate treatment. Jowett examined the sinuses in 500 cases of mental disease. He found infection of the nasal sinus in only 7.6 per cent of the cases. In a series of 184 mentally normal persons used as a control, sinus suppuration was found to be present in no less than 5 per cent. Commenting on the fact that pioneer workers in the field claimed a higher incidence, Jowett states that subsequent investigations may prove that the incidence of sinus infection is much lower; however, even the occurrence of infection in 10 per cent of cases demands attention and treatment. His work shows that the incidence of sinus disease is no greater in patients with mental illness than in the general population. For this reason the relationship to mental disease as an etiologic factor remains obscure.

KASANIN, Chicago.

PROLONGED NARCOSIS IN MANIC-DEPRESSIVE PSYCHOSIS. T. J. HENNELLY, J. Ment. Sc. **82**:608 (Sept.) 1936.

Hennelly reports the results of treatment in 88 cases of manic-depressive psychosis and compares them with the results in a series of 133 cases reported previously by Ström-Olsen and Muriel McCowan (*J. Ment. Sc.* **80**:658 [Oct.] 1934). In Hennelly's series 36.3 per cent of patients recovered; 29.5 per cent improved, and 33.8 per cent showed no change. There is thus a striking resemblance in the results to those in the series of cases reported previously. Recovery and improvement were most striking in the cases of the manic type. The routine of treatment consists in giving intramuscular injections of 2 cc. of the diethyldiallyl barbiturate of diethylamine (Somnifaine) twice a day. Each injection is accompanied by the subcutaneous injection of from 10 to 15 units of insulin, dextrose being given freely. Hennelly warns that the urine should be examined every day, as acetonuria develops in 50 per cent of cases. When this is found, the dose of insulin should be increased. If acetone persists, the treatment should be discontinued. Hennelly stresses that the hypnotic should never be given in toxic or delirious states. By judicious administration of this treatment, the attacks can be terminated within two or three weeks.

KASANIN, Chicago.

DEVELOPMENT OF MENTAL DISTURBANCES IN RELATION TO CURRENT EVENTS. H. CLAUDE, P. SIVADON and J. FORTINEAU, Ann. méd.-psychol. **94**:247 (July) 1936.

It is generally admitted that external events are in themselves not sufficient to create a psychosis. They supply merely the material for the delusional content of various typical psychoses, without causing them. However, there are numerous instances of acute psychotic manifestations in the development of which the exogenous emotional factors often play an important rôle. The authors point out the striking increase in the number of men admitted for acute mental disturbances coincident with recent political events in France. Thus, for June 1936 the number of men admitted to St. Anne's hospital in Paris was 240, as against 165 in June 1935. The authors report two typical cases of middle-aged factory workers in whom there developed an anxiety state with delusional interpretation of current events (general strikes) in which they were directly involved. Both were free from hallucinatory manifestations. In both instances there was evidence of a constitutional psychic fragility. Although both patients in the past had repeatedly been subjected to various situation difficulties, they were able to withstand the emotional strain until recent social conflicts placed them in a state of material insecurity and great emotional exertion. Without these events they would have had every chance to maintain their psychic emotional balance. YAKOVLEV, Waltham, Mass.

PSYCHOLOGIC STATE OF CHOREIC PATIENTS. WOLFGANG HOCHHEIMER, J. f. Psychol. u. Neurol. **47**:49, 1936.

Hochheimer studied in detail the mental condition of six patients with Huntington's chorea, three of whom were in the early stages of the disease and three in a far advanced stage. In the early stages the diagnosis of a specific dementia could readily be established. The dementia was characterized by the inconstancy of its manifestations. There were periods, varying in duration, during which the patients succeeded well; they could express themselves and apparently could think correctly. They were by no means devoid of all "intelligence"; they could size up a situation and had good insight. Not until the last stages of the disease did the dementia and intellectual defect become complete.

In patients with far advanced chorea, speech was greatly impoverished and was abrupt, poorly articulated and telegraphic. An attempt to speak for any length of time was associated with such difficulties in articulation that speech became utterly unintelligible. When these patients were requested to repeat what they had said, they became irritable and merely shouted out the same words more loudly, without rendering themselves more intelligible. The more they were urged to express their thoughts in language, the more mute they became. Occasionally they attempted to extricate themselves from the dilemma by confabulation and circumlocution. In this struggle to make themselves understood, they lost the trend of thought and wandered into other spheres of thought wholly irrelevant to the subject-matter to which their attention had originally been directed. Some of the patients' answers to questions were characterized by a certain amount of stereotypy and substitution of words.

In both groups of patients it was evident that there was marked disturbance of all motor and thinking processes. In the final stages of the disease there was loss of orderly continuity of thought, speech and action, so that adequate contact with the outside world was entirely severed. The patients' interests in life became progressively narrower and were finally reduced to those of the lowest primitive animal life. The dementia became complete. KESCHNER, New York.

NEUROSIS AND CRIMINALITY. M. MÜLLER, Schweiz. Arch. f. Neurol. u. Psychiat. **36**:112, 1935.

Although a complete analogy may exist between certain criminal acts and neurotic symptoms, it is doubtful whether a neurosis of itself can activate latent criminal tendencies, however important a part it may play in determining the

character of overt acts. Sadistic and aggressive tendencies are common in neurotic persons, but, compensated as they generally are by a highly developed superego, these tendencies rarely lead to the commission of crime. Since a mild mental defect or a poorly developed ethical sense, either of which would alone account for the asocial behavior, can be demonstrated in the majority of neurotic criminals, cases suitable for consideration in the present study are relatively rare.

Two cases are presented of stealing without apparent motive by persons of good moral character, both of whom were neurotic. The overt act in the one seemed to represent the vicarious gratification of a submerged impulse, whereas in the second it was attributed to an unconscious feeling of guilt and the consequent desire for punishment. The activation of the asocial tendencies, however, was ascribed to a menstruation psychosis, in the first case, and to a twilight state, in the second. Müller expresses the view that these activating factors were accidental and independent of the neurosis itself. Numerous cases of this type must be studied carefully before their social and legal implications can be given proper consideration.

DANIELS, Denver.

ALIMENTARY HYPERGLYCEMIA IN MANIC-DEPRESSIVE PSYCHOSIS. H. I. SCHOU, Acta psychiat. et neurol. **10**:565, 1935.

Schou studied alimentary glycemia in ten cases of "undoubted" and in eighteen cases of "doubtful" manic-depressive psychosis. A rise of blood sugar to 200 mg. or more per hundred cubic centimeters, with a fall to not below 120 mg. after two hours in at least three tests on each person was considered as positive evidence of an abnormal hyperglycemic reaction. From the results thus obtained (in eight cases), Schou concludes that manic-depressive persons over 35 years of age always show an abnormally high and protracted curve for blood sugar. The curves for manic-depressive patients show a much wider variation in the values for sugar than the curves for normal persons. In "doubtful" manic-depressive psychosis the incidence of "positive" curves for blood sugar is approximately half as high as in "undoubted" manic-depressive states. The reaction of the blood sugar in patients with manic-depressive psychosis to sedatives was not different from that of normal persons and abnormal (epileptic) patients used as controls. During the manic phases the curves were higher and declined more slowly during the depressed phases. In a number of manic-depressive patients the abnormal alimentary hyperglycemia tended to subside simultaneously with clinical improvement. This has a prognostic value.

YAKOVLEV, Palmer, Mass.

Diseases of the Brain

VERTIGO IN BRAIN TUMORS, WITH ESPECIAL REFERENCE TO RESULTS OF LABYRINTH EXAMINATION. E. A. SPIEGEL and A. ALEXANDER, Ann. Otol., Rhin. & Laryng. **45**:979 (Dec.) 1936.

The observations of Spiegel and Alexander on tumor of the brain seem to corroborate the assumption of a representation of the labyrinth in the cerebral cortex, particularly in the temporal lobe. Parts of the frontal lobe, especially the centro-opercular region, must also be taken into consideration as a place at which vestibular and spinal impulses joined in the subcortex (cerebellorubral system) may enter. The concept that vertigo in association with tumor of the brain is only a general symptom of increased intracranial pressure seems to need revision. In a large number of cases symtoms of choked labyrinth, hyperexcitability of this organ, differences in excitability between the two sides, nystagmus, diplopia and cerebellar disturbances are found, and the appearance of vertigo is explainable as due to these effects of increased intracranial pressure. Yet there remains a group of cases in which such an effect of pressure on the labyrinth or on the brain stem is absent. In these cases, at least, it seems not unreasonable to assume that the vertigo may appear as a local symptom of the cerebral cortex due to direct lesion (stimulation)

of the aforementioned cerebral areas or to pressure on these foci by a tumor in a neighboring region. In general it seems that a tumor close to the sylvian fissure induces vertigo more easily than does a tumor more distant from this fissure.

EDITOR'S ABSTRACT. [J. A. M. A.]

THE INCIDENCE OF THE CLINICAL TYPES OF NEUROSYPHILIS IN MALES, IN PREGNANT AND IN NON-PREGNANT FEMALES. W. C. MENNINGER and J. E. KEMP, J. Nerv. & Ment. Dis. **83**:275 (March) 1936.

In 400 cases of neurosyphilis 38 per cent of males showed asymptomatic neurosyphilis, 56 per cent parenchymatous and 6 per cent meningovascular; 63 per cent of nulliparas had the asymptomatic type, 29 per cent the parenchymatous and 8 per cent the meningovascular, and 54 per cent of multiparas showed the asymptomatic type, 38 per cent the parenchymatous and 8 per cent the meningovascular. Nulliparas showed a preponderance of cases in the third decade and a very small percentage after 40 years of age. In contrast, men and multiparas showed the peak in the fourth decade, with a much higher incidence after this period than nulliparas. The preponderance of nulliparas in the earlier age group may be due to the fact that the majority are unmarried and probably much more frequently exposed to infection. Males do not present themselves for diagnosis until a later age than nulliparas, and then more often because of symptoms demanding attention. The smaller percentage of parenchymatous neurosyphilis in multiparas may be due to the protective effect of pregnancy against the development of neurosyphilis.

HART, New York.

NEUROLOGICAL ABNORMALITIES PRODUCED BY ELECTRICITY. ORTHELLO R. LANGWORTHY, J. Nerv. & Ment. Dis. **84**:13 (July) 1936.

Experimental studies have shown that severe damage of nerve cells and nerve fibers may be produced by electric shock. These changes are observed most clearly if the subject survives for a few days and are intensified after repeated exposures to the current. They are obviously most severe in parts directly traversed by the current, although it is difficult to determine the course of the current through the body at the time of an electric shock. Since the extremities most commonly make contact with the current, it is obvious that the spinal cord is more likely to be damaged than the brain. Spinal lesions have been most frequently reported as chronic abnormalities following electric shock in man. Similar abnormalities can be produced experimentally in animals, and in such cases pathologic studies have been made. The cases of so-called disseminated sclerosis following electric shock probably belong to this category of damage to the spinal cord. Since any group of cells may be injured by electricity, the resultant neurologic lesions are necessarily complex and may involve any portion of the nervous system. The amazing thing is the rarity of late symptoms in the great majority of cases of electric shock. This is perhaps best explained by the fact that injured cells are scattered among others which appear normal. Experimentally, a series of shocks produce a large percentage of neurologic injuries.

When a patient is seen immediately after an accident in severe shock, with paralysis of respiration, it is important to realize that there may be a temporary block of nerve conduction, and artificial respiration should be continued for a considerable period, in the hope that the fatigued cells of the respiratory center will function again.

Fissuration in the cortex, with swelling of the ganglion cells, was observed by Hassin in the brains of five electrocuted criminals. Cataracts and lesions of the cornea have been reported. Paralyses, usually of the legs, hemiplegia in association with arteriosclerosis, disorders of speech, loss of taste, atrophy of the optic nerve, transient papilledema, vestibular damage and changes in the spinal cord resembling the picture of progressive muscular atrophy have all been reported after electric shock.

HART, New York.

THREE CASES OF MIND BLINDNESS (VISUAL AGNOSIA). J. M. NIELSEN and KARL O. VON HAGEN, J. Nerv. & Ment. Dis. **84**:386 (Oct.) 1936.

Munk first detected mind blindness in dogs by demonstrating that removal of a certain portion of the occipital cortex gives rise to cortical, or perceptual, blindness. Animals could detect the presence of objects but could not recognize even familiar objects by vision alone. Ferrier concluded that the area of the cortex concerned chiefly with the recognition of words is the left major angular gyrus.

Nielsen and Von Hagen describe three cases of visual agnosia, the condition in the first being due to an organic vascular lesion, either embolic or thrombotic, which produced softening of the occipital lobes, that in the second to encephalitis, probably with softening, and that in the third to drugs, such as allylisopropylbarbituric acid with amino pyrine (allonal) and bromide. In all three cases there was marked difficulty in recognizing objects seen, but when the object was associated with olfactory, auditory or tactile impressions, it was recognized. In the last case visual agnosia disappeared after withdrawal of the drugs.

HART, New York.

BRAIN TRAUMA. N. W. WINKELMAN and J. L. ECKEL, J. Nerv. & Ment. Dis. **84**:399 (Oct.) 1936.

Change of personality is a sequel to trauma of the brain that is not easy to estimate. Convulsions as a rule occur relatively late after trauma; why they occur in some persons and not in others is not clear. Possibly the trauma lowers the threshold to convulsions. It is known that trauma can activate a latent syphilitic infection, and it is conceivable that it may also aggravate other organic diseases of the nervous system. Unfortunately, clinical examination does not reveal sufficiently the damage to the brain, even when extensive. Meyer in 1904 observed small foci of softening with cortical hemorrhages, especially in the frontal and temporal areas, and absence of marginal glia beneath the pia at the points of injury. Diffuse glial alterations occurred, with small foci of degeneration throughout the brain. Neuburger expressed the belief that trauma causes "irritability" of the circulation and that vasospasm occurs, resulting in areas of softening.

Winkelman and Eckel described in considerable detail five cases of trauma to the brain. Three types of changes could be differentiated: (1) changes resulting directly from the injury itself; (2) changes secondary to the injury, and (3) processes in the brain associated with the terminal illness. Clinically, the most common manifestations were changes in personality and convulsive seizures. Focalizing signs and symptoms were present in only one case. Histologically, there were focal lesions of hemorrhage and softening, with scattered petechial lesions. Adhesions of the pia-arachnoid to the cortex and the dura were present in nearly all cases. An abscess developed at the point of impact in a patient with disease of the middle ear of long standing, generalized convulsions having occurred seven days after the injury, although signs of increased intracranial pressure did not occur until three years later.

HART, New York.

PROGRESSIVE DEMENTIA, WITHOUT HEADACHE OR CHANGES IN THE OPTIC DISCS, DUE TO TUMOURS OF THE THIRD VENTRICLE. GEORGE RIDDOCH, Brain **59**:225, 1936.

The presence of progressive dementia in the absence of severe headache, vomiting and either papilledema or atrophy of the optic nerve is an uncommon occurrence with intracranial tumor in any situation when the illness has lasted for a considerable time. It is even more uncommon with tumor of the third ventricle. Riddoch reports two exceptional cases of tumor of the third ventricle in which there was no headache, vomiting or alteration of the optic disks or visual fields.

In the first case a round colloid cyst was attached to the choroid plexus. It lay bind the foramina of Monro, which were grossly enlarged, and well in front of the aqueduct of Sylvius, which was narrowed and flattened from above downward. The cyst bulged into the lateral ventricles, from which it was separated by the roof of the third ventricle. The quadrigeminal plate was flattened by com-

pression from the overlying, greatly enlarged posterior parts of the lateral ventricles. This explains the involvement of the aqueduct in the hydrocephalus, as well as the irregularities of the pupils. The obstruction of the aqueduct could not be due to the tumor, when its position is considered. The size of the tumor alone may have impeded the flow of fluid through the third ventricle, thus explaining the hydrocephalus involving the lateral ventricles. It is probable that the tumor caused intermittent obstruction of the foramina of Monro, in which case the increased size of the foramina would be compensatory. In the second case a tumor was present in the posterior part of the third ventricle, which histologic examination showed to be a spongioblastoma multiforme. The cerebral convolutions were flattened, and the lateral ventricles were greatly dilated.

These cases illustrate the fundamental importance in clinical neurology of the time factor, which determines the presence or absence of many symptoms and bears much on the evolution of the illness. When pressure within the skull is raised rapidly, headache is an almost immediate complaint, before consciousness is lost, and papilledema, often with hemorrhages, develops within a short time. On the other hand, slowly increasing pressure from a tumor, whether local or general, may for long be unassociated with either of these symptoms. Progressive dementia, without headache or papilledema, may occasionally result, however, from invasion of both frontal lobes and the anterior part of the corpus callosum by an infiltrating glioma or a centrally placed meningioma, but the dissociation and its duration are again dependent on the rate of development of the pathologic process.

While not primarily concerned with the mechanism by which these disorders of function are produced, Riddoch is of the opinion that the fact that great improvement may follow relief from compression by removal of its cause is in favor of the view that impairment of blood supply is the primary factor. In the causation of the headache, gross variation in tension in the vessels, especially the arteries, the venous sinuses and the dural septums probably plays an important part.

In the two cases reported, few symptoms of involvement of the hypothalamus were present. This is not surprising, for the floor of the third ventricle was not directly involved by the growth in either case. Abnormal drowsiness, so common with a lesion in this region, was a prominent feature in both cases. Fulton and Bailey (1929) expressed the belief that the neural mechanisms concerned with regulation of sleep lie in the posterior part of the hypothalamus, close to the midbrain. That the anterior part of the midbrain was involved in each case is shown by the pupillary abnormalities, including reflex iridoplegia. However, since the lethargy appears from the first to have been associated with mental dulness, it is safer to assume that it was a general rather than a focal symptom.

SALL, Philadelphia.

PRESENT STATE OF THE POSTTRAUMATIC SUBJECTIVE SYNDROME FOLLOWING INJURIES OF THE HEAD SUFFERED DURING THE WAR OF 1914-1918. RENÉ TARGOWLA, Ann. méd.-psychol. **94**:153 (July) 1936.

Targowla reports the result of a survey of the present subjective state of war veterans who suffered injuries of the head during the World War. Only veterans who suffered concussion or presented a bone defect in the skull were included in the study. Targowla comes to the conclusion that whenever the subjective syndrome (headache, vertigo, emotional instability, insomnia, fatigability and diminution of memory) developed as the only sequel of the injury to the head, it practically always disappeared within three years after the injury. If the subjective syndrome persisted or reappeared subsequent to that period, it was due in 175 of 180 cases to entirely new and independent etiologic factors; among these factors aging of the patients, with beginning arteriosclerosis and increased blood pressure, was most common. That the past injury to the head had no bearing on these vascular changes is shown by the fact that of the persons who suffered mere concussion and applied for compensation because of the subjective syndrome, often as late as ten or more years after the injury, 73 per cent showed increased blood pressure, whereas of persons with severe injury to the head and permanent organic

sequelae less than 30 per cent showed a high blood pressure. Targowla points out that the existing French law on compensation inspired by the sentiment of "national gratitude" does not provide for differentiation between the direct consequences of injury to the head suffered during the World War and the subjective syndrome arising as the result of independent pathogenic factors occurring during the twenty years following the injury. Compensations often are granted on the mere record of an injury.

YAKOVLEV, Waltham, Mass.

HEREDITARY CHARACTER OF NEUROFIBROMATOSIS OF VON RECKLINGHAUSEN. C. H. SCHRÖDER, Beitr. z. klin. Chir. **164**:563 (Dec. 23) 1936.

According to Schröder, the multiplicity of symptoms of Recklinghausen's disease is simplified by the grouping proposed by Ferdinand Curtius, according to which all its manifestations are divided into three groups: (1) multiple tumors of the skin (fibromata mollusca), frequently associated with tumor of the nerves; (2) anomalies of pigmentation of the skin, particularly small or large pigmented nevi referred to as coffee spots, and (3) psychic disturbances, particularly imbecility, and, more rarely, psychoses and psychopathies. Among other symptoms are mentioned skeletal changes, kyphoscoliosis, asymmetry of the skull, thickening or rarefaction of bones and subperiosteal cyst. The bones may undergo decalcification or an abnormal increase in calcium. Pseudarthroses are noted in childhood. Another peculiarity is a keloid-like hypertrophy of scars, while disturbances of the glands of internal secretions may lead to hypogenitalism, acromegaly, myxedema, hyperthyroidism and Addison's disease. Histologic study of the multiple tumors reveals neuroma, neurofibroma or pure fibroma. The origin of the tumors is to be seen in faulty differentiation of mesenchymal tissue from the ectoderm. The embryonic origin of the disease is indicated by its hereditary character. Of the 466 cases reported in the literature, a hereditary character was present in 18 per cent of those occurring in children and in 16 per cent of those in adults. The author reports the observation of a family in which hereditary transmission of the disease as a dominant trait was traced for three generations. A father and twin sisters exhibited anomalies of pigmentation and characteristic tumors confirmed by histologic examination. Four other members of the family exhibited an abortive type of the disease in the form of typical anomalies of pigmentation of the skin, namely, the so-called coffee-spots. In one case the tumor had an unusual location under the tongue. Two cases of imbecility were present in relatives. Seven of the affected persons presented similar anomalies of pigmentation, while three showed a rather large single tumor. Similarity in the symptoms and the development of the diseease suggests the existence of a familial type of the disease.

EDITOR'S ABSTRACT. [J. A. M. A.]

MEASUREMENTS OF HEAT PRODUCTION IN CASES OF CEREBRAL HEMIPLEGIA. P. E. BECKER, Deutsche Ztschr. f. Nervenh. **141**:279, 1936.

The heat production of the legs in cases of hemiplegia was determined by a simplified calorimetric method, using final temperature levels for periods up to two hours and comparing at the same time the temperature of the normal with that of the paralyzed extremity. In patients with a lesion of the internal capsule the heat production of the paralyzed limb is usually diminished as compared with that of the other side. In patients with a lesion of the frontal lobe there is always an increase in the heat production of the affected leg. The type of disturbance in heat production is independent of the tonus of the paralyzed muscles but is parallel to the severity of the paralysis.

HOEFER, Boston.

PATHOGENESIS OF MULTIPLE SCLEROSIS. B. DATTNER, Wien. klin. Wchnschr. **50**: 87 (Jan. 22) 1937.

Dattner discusses the present status of knowledge on the pathogenesis of multiple sclerosis, pointing out that it is not definitely known as yet. He cites

various theories and describes his own studies on the problem. He admits that there is a bewildering mass of factors and observations, the organization of which is extremely difficult. First, there is the fact that in the great majority of cases of multiple sclerosis there exist hematic changes which can be demonstrated not only by means of the complement fixation reaction for tuberculosis but also by means of an alcoholic cerebrospinal extract, so that they can hardly be regarded as specific. Then it has been shown that the blood of patients with multiple sclerosis shows lipolytic substances and higher diastase values, factors which indicate hepatic impairment. Further, it has been demonstrated that the coagulation time of the blood of patients with multiple sclerosis is considerably prolonged and more unstable than that of normal persons, which apparently likewise indicates hepatic impairment, perhaps a disturbance in the fat metabolism. Systematic investigation of the gastric secretion of patients with multiple sclerosis revealed not only anacidity or hypacidity in a considerable percentage of cases but also hyperacidity—that is, conditions similar to those which have been observed in pellagra and beriberi. Moreover, in a considerable number of cases hematic changes were observed which were on the borderline of hyperchromic or hypochromic anemia. Finally, the symptomatology as well as the clinical course indicated many similarities to such avitaminoses as pellagra, beriberi and scurvy. Dattner shows that all these observations give rise to questions that cannot be answered on the basis of the present status of knowledge. At any rate, he considers careful analysis in individual cases in the various directions as an aid in obtaining a better insight into the pathogenesis of multiple sclerosis.

EDITOR'S ABSTRACT. [J. A. M. A.]

EPILEPSY AND HEREDITARY DISPOSITION: II. INCIDENCE OF EPILEPSY IN SIMILAR MONOZYGOTIC TWINS. K. CONRAD, Ztschr. f. d. ges. Neurol. u. Psychiat. **155**:254 (April) 1936.

Conrad presents detailed case histories as a supplement to his previous statistical studies on the incidence of epilepsy in the twin (similar or dissimilar) of a patient with epilepsy. These studies establish the role of the genetic factor in the pathogenesis of epilepsy. The presentation of individual case histories corroborates in a concrete way the conclusions based on statistical data, which otherwise give the impression of unreality and impractical generalizations. These case studies also permit more accurate estimation of the relative roles of genetic and environmental factors. The study of monozygotic twins, in whom the genetic factor is identical and therefore constant, affords an exceptional opportunity to study the interplay of exogenous and endogenous determinants. The chances that identical twins will present similar pictures because of exposure to precisely the same external nocuous agents are so small (1:240,000,000) that the objection to the use of this method of approach can be disregarded.

Eight cases of epilepsy in both of monozygotic twins in which the course of the disease was very similar are presented in detail, as well as brief résumés of ten reports from the literature. In most of the cases there was a history of mental disease, mental deficiency, epilepsy, alcoholism, migraine or psychopathic personality in close relatives. The grand mal seizures were often preceded by long periods during which absence of attacks, migrainous seizures and enuresis occurred. Sometimes a history of convulsions in childhood was obtained. The attacks usually began between the ages of 5 and 15, and, more rarely, up to about 26. In almost all cases the attacks appeared spontaneously and in reaction to no known external circumstances. Trauma to the head was often the result rather than the cause. A striking similarity in the attacks, aurae, interparoxysmal complaints, ages of onset and the nature of the mental deterioration are strong arguments for the endogenous nature of this disease. The attacks were at first infrequent. Later they came more often, and intellectual deterioration and dementia developed rapidly. This clinical picture is characteristic of the genetically determined form of epilepsy and can be proved for practical purposes (sterilization), even in the absence of

other instances of epilepsy in the immediate family. Conrad disagrees with Mauz and others who laid emphasis on the necessity for the existence of changes in personality and the mental state as a criterion for the diagnosis of idiopathic epilepsy.

A case of a pair of twins with epilepsy and mental deficiency is reported by Conrad, with descriptions of five others from the literature. Four cases in which epilepsy and focal disorders occurred in both twins were found in the literature. Conrad considers the epilepsy, mental deficiency and focal signs as symptomatic of a hereditary developmental defect of the brain. He suggests that many cases of so-called idiopathic epilepsy may belong in this group of dysplasias of the brain. In these instances the anatomic defects are neither gross nor located in significant parts of the brain.

Conrad also describes five of his own cases and five instances from the literature in which the clinical course and character of the convulsive state differed in identical twins. Differences in endocrine status, the degree of dementia and the existence of focal signs were also present. The more mature of the twins, as well as the left-handed members, were usually the more seriously ill. In a few cases epileptic equivalents alone were present in one of the twins. A number of hypotheses are offered as an explanation for the differences in epileptic twins: 1. Difference of cytoplasm is a possibility, on the basis of recent evidence that the cytoplasm plays a role in the transmission of hereditary characteristics. The milieu of the gene is apparently of some importance. 2. The absence of exogenous factors which usually favor the active participation of the particular gene in the development of the individual organism. 3. Exogenous factors not affecting both twins at the same time are important. Injuries to the head, syphilis, endocrine disorders and sunstroke, and even different reactions to the attacks themselves, are all mentioned. There is no doubt that differences in the vascular changes (spasms) accompanying the attacks may have bearing on the incidence and frequency of subsequent convulsive seizures. 4. The fortuitous presence of other inhibiting genes, which prevent the appearance of a given characteristic, must also be considered. The author warns against the use of any single criterion by which to judge the presence or absence of hereditary epilepsy. Individual differences exist, and the particular condition must be evaluated in the light of the course of the illness, the make-up of the subject and the family background.

SAVITSKY, New York.

EPIDERMOIDS OF THE CENTRAL NERVOUS SYSTEM. W. MAHONEY, Ztschr. f. d. ges. Neurol. u. Psychiat. **155**:416 (May) 1936.

Mahoney reports five cases of epidermoid of the nervous system. The first case was that of a pearly tumor in the left cerebellopontile angle, compressing the brain stem and containing nerve fibers. The second case was that of a man aged 27 with a pearly tumor in the right cerebellopontile angle. It pushed the pons to the left and exerted traction on the middle cerebellar peduncle. It extended anteriorly, displacing the cerebral peduncle and reducing the aqueduct to a slit, and pushed up against the floor of the third ventricle. The amount of distortion of the brain stem was unusual. The symptoms of hypothalamic involvement in this case are worthy of note (obesity, somnolence and manic excitement). The cochlear part of the eighth nerve remained unaffected, while there was evidence of functional impairment of the vestibular portion. The disturbance in equilibrium was probably due to the marked compression of pontocerebellar pathways. The third case was that of a tumor in the left cerebellopontile angle with marked distortion of the brain stem and the left side of the cerebellum. Crystals of cholesterol were observed in the trigeminal nerve. In the fourth case, that of a woman aged 53, an epidermoid was observed in the right side of the pons, compressing the right side of the cerebellum and extending upward and anteriorly into the right temporal lobe, to the level of the third nerve. On the right side there was

a cystic extension of the tumor from the cerebral peduncle to the optic chiasm and the sylvian artery. The fifth case was that of a man aged 27 with an extradural epidermoid extending through the skull, with marked compression of the left cerebral hemisphere. The tumor looked like a biconvex lens, with a maximum thickness of 5 cm.

Mahoney collected from the literature 142 unquestionable cases of epidermoids; the tumor in 23 instances was diploic in origin; in 7, intraspinal; in 15, in the fossa rhomboidea; in 44, parapituitary, and in 53, parapontile. In the series of 2,500 tumors reported by Cushing there were 15 epidermoids (0.6 per cent), and 5 instances of this tumor (0.66 per cent) were found in Foerster's series of 750 cases. The tumor may become manifest clinically at any age. It has been recorded in patients of ages from 1½ to 78 years. The average age was 35. In 132 cases in which data are given, 76 occurred in males and 56 in females. Trauma plays no role in the etiology, though the thinness of the bone at the site of the extradural epidermoid may predispose to injury of the skull.

The accepted theory of the pathogenesis of this tumor is that of development from misplaced embryonic epidermal cells. Mikulicz in 1876 suggested the possible origin of a tumor of the parapontile group from cells orginating from the anlage of the inner ear, which early in embryonic life lies near the trigeminal root. No case has yet been reported in which such a tumor was closely connected with the endolymph system. Bonorden in 1892 postulated the origin of a tumor of the parapituitary group from epidermal tissue in a tumor of Rathke's pouch. Verse in 1918 reported a case in which an epidermoid was connected with such a tumor of the hypophysial duct. Bostroem stated that the sites of predilection of the tumor can be related to points of transition from one part of the embryonic brain to the other.

In the clinical study of these cases the author noted the unusual frequency of mental symptoms, even in cases in which the tumor was in the posterior fossa. The prominence of facial pain in the history is also noteworthy. Somnolence is not infrequent and may be due to "chemical" encephalitis resulting from irritation by cholesterol. This theory perhaps may explain also the mental symptoms in some cases. The high incidence of convulsions (30 per cent in cases of parapontile tumor) may be explained in the same way. Visual disturbances were found in a relatively small number of cases (7 of 44) of the parapituitary type. Olivecrona noted the tendency of this tumor to extend into and widen the optic foramen. Nagel in 1923 diagnosed an epidermoid of the fourth ventricle by observing crystals of cholesterol and desquamated cells in the spinal fluid.

There is record of operation in only 30 per cent of 112 cases. In 11 of these instances the patient survived the operation (operative mortality, 67 per cent). Cushing reported 6 cases in which operation was successful and Olivecrona, 2. Esmarch (1865) reported the first case of successful removal of an epidural epidermoid. Seventeen of 19 other patients recovered. Bailey in 1920 reported the first case in which there was successful removal of intracranial intradural tumors of this type. These occurred in the fourth ventricle and the parapituitary region. Anschutz in 1927 recorded the first case of a parapontile tumor in which recovery followed operation.

Experimental injection of cholesterol into a dog resulted in no clinical symptoms for six months. When the animal was killed, the ganglion cells at the site of injection of the cholesterol were observed to be degenerated. No diffuse encephalitic or meningitic changes were noted.

SAVITSKY, New York.

SIX CASES OF TRAUMATIC ANOSMIA AND AGEUSIA. J. HELSMOORTEL JR., R. NYSSEN and R. THIENPONT, Acta psychiat. et neurol. **11**:251, 1936.

Several authors have drawn attention recently to the frequency of anosmia in cases of injury to the head. Since taste is the result of gustatory perceptions combined with olfactory sensations, it is to be expected that complete anosmia will

lead to partial impairment of the sense of taste without loss of elementary gustatory sensations (sweet, bitter, salty and acid). Ageusia, i. e., more or less total loss of elementary gustatory perceptions, is nevertheless far less frequent than anosmia. In more than one hundred cases of injury to the head the authors encountered only six instances in which anosmia was associated with loss or diminution of perception of the elementary savors. In none of the cases did ageusia exist without anosmia. In two cases in which the disturbances of the two special senses regressed, recovery of the elementary gustatory sensations either followed or was simultaneous with recovery of olfactory sensations. In only one of six cases were there spontaneous and subjective gustatory hallucinations of a sweet taste (glycogeusia). These disappeared gradually and simultaneously with the objective ageusia. The authors conclude that in at least five of the cases reported the ageusia is best explained as the result of autosuggestion. They point out that, according to Bechterew, Kleist and others, the cortical gustatory representation is localized in the rolandic operculum of each hemisphere and that each gustatory area receives impressions from both halves of the tongue, although prevalently from the contralateral side. To explain anosmia with ageusia as the result of an organic lesion, one would need to postulate at least three widely scattered lesions, two situated on the convexity of each hemisphere (opercula) and one in the base of the brain (hippocampus). Even if one assumes that the gustatory center is in the vicinity of the olfactory area in the hippocampal gyrus, the nonexistence of isolated ageusia and the parallelism in the evolution of anosmia and ageusia indicate that the latter is subordinated to the former. Moreover, the fact that in five of six cases evidence was shown of personality traits of a hysterical type, with a tendency to abnormal hypersuggestibility, pleads in favor of the view that ageusia is merely a functional complication of traumatic anosmia. YAKOVLEV, Waltham, Mass.

EIGHTEEN CASES OF EPILEPSY WITH FITS IN RELATION TO SLEEP. GUDMUND MAGNUSSEN, Acta psychiat. et neurol. **11**:289, 1936.

Magnussen reports his observations on the incidence of epileptic seizures in relation to sleep. He believes that there exists a type of epilepsy characterized by the occurrence of seizures exclusively or prevalently in a constant time relationship to the hypnic phase of the wake-sleep cycle. He proposes to call this type of epilepsy "hypnosepilepsy." Eighteen cases in which this type of seizure was shown were selected for study of factors which may underlie the relationship between sleep and seizures. The material is divided into four groups: Group A consisted of five men for whom the curve for the incidence of seizures was characterized by two peaks—the highest peak being in the period between 9 p. m. and 2 a. m. and the second, lower peak between 3 a. m. and 8 a. m. Group B consisted of five women who indulged in afternoon naps. In this group three major peaks were found in the incidence of seizures—one was between 1 and 3 p. m. and the second and third were similar to those in group A. In group C, which consisted of four men and two women, one major peak occurred in the period between 5 and 8 a. m. Group D was represented by one woman, the incidence of whose seizures showed two major peaks—one in the afternoon (between 1 and 3 p. m.) and another at the time of awakening (between 6 and 8 a. m.). Magnussen believes that in such cases sleep is one of the most important factors in the provocation of seizures. The number of seizures is on the whole proportional to the depth of sleep. He believes that the biochemical shifts in the carbon dioxide tension of the blood may be responsible for the occurrence of the seizures, either on account of the speed of the shift or through its absolute magnitude. In a study of nocturnal variations in the blood sugar made at intervals of one hour on eight of his patients, Magnussen observed a striking lability of the sugar level of the blood with a tendency to hypoglycemia; however, no relationship was found between the lowest level of the sugar and the incidence of seizures. YAKOVLEV, Waltham, Mass.

Treatment, Neurosurgery

General Paresis Treated by Mosquito-Inoculated Vivax (Tertian) Malaria. Ernest Kusch, D. F. Milam and W. K. Stratman-Thomas, Am. J. Psychiat. **93**:619 (Nov.) 1936.

Better results were obtained with malaria therapy when the patient was infected directly by a mosquito bite than when he was inoculated with infected blood. A strain of the mosquito infected with tertian malaria (Plasmodium vivax) was cultured for this purpose. The malaria so induced has an incubation period of from eleven to fourteen days, and about half the patients had spontaneous remissions. The others responded promptly to quinine. Because the mosquito-induced malaria is milder than the blood-produced form, it is possible to allow more chills and to secure better clinical results. Thus, in a series of patients with blood-inoculated malaria the number of paroxysms per patient varied from 8 to 12. In the group of patients bitten directly by the mosquitoes the number of paroxysms varied from 17 to 24. Similarly, the proportion of remissions was 19 per cent for the blood-inoculated group and 26 per cent for the mosquito-infected group. In the former group 7 per cent of the patients died, presumably from the malaria. None of the mosquito-infected patients died. The proportion who improved or who reached a remission totaled 75 per cent in the series of patients who were bitten directly by the insect and only 55 per cent in the blood-inoculated group. The authors conclude that when proper facilities are available, the treatment of dementia paralytica by malaria induced by mosquito bite is the technic of choice.

Davidson, Newark, N. J.

Dermatitis Due to Tryparsamide. Saul S. Robinson, Arch. Dermat. & Syph. **34**:251 (Aug.) 1936.

Robinson reports a case of tryparsamide dermatitis in a woman aged 34 who was suffering from cerebrospinal syphilis. She had previously received twelve injections of neoarsphenamine, each of which was followed by nausea, vomiting, chills and fever lasting from twenty-four to forty-eight hours. No pruritus or dermatitis resulted from the drug. Four years later, eighteen injections of tryparsamide were given, the dose ranging from 0.5 to 2 Gm. After the sixteenth injection, she noticed an itching eruption over the upper part of the trunk and arms. The severity of the cutaneous reaction increased with each succeeding injection, and a diffuse erythematous, maculopapular, scaly eruption appeared. Patch tests with a concentrated solution of tryparsamide gave a positive reaction over the involved area but negative reactions at other sites on the patient's body. After the intravenous administration of calcium thiosulfate the lesions disappeared.

Davidson, Newark, N. J.

Bulbocapnine in the Treatment of Behavior Disorders Such as Occur in Chronic Epidemic Encephalitis. R. L. Jenkins and C. C. Rowley, J. Nerv. & Ment. Dis. **84**:507 (Nov.) 1936.

The effect of the administration of bulbocapnine on the behavior of nine adolescent boys afflicted with the behavior disorders typical of chronic epidemic encephalitis was observed under controlled conditions. In five cases there was a history of acute illness which was diagnosed as epidemic encephalitis. In two cases there was a history of acute illness which, considering the present physical findings, may fairly be diagnosed in retrospect as epidemic encephalitis. In two cases there was no evidence in favor of the diagnosis other than the characteristic behavior syndrome. Bulbocapnine was administered as a routine, orally or hypodermically, three times a day after meals, in doses of 0.1 and 0.2 Gm. Careful comparison of daily records of the behavior kept by physicians and attendants failed to reveal evidence that bulbocapnine was of value as administered to these boys.

Hart, New York.

A Study of the Use of Coramine in Dealing with the Effects of Barbituric Acid Derivatives. Purcell G. Schube, New England J. Med. **214**: 926 (May 7) 1936.

Barbituric acid preparations are used to produce unconsciousness, which may be recognized as simple sleep. At times unsafe reactions occur. The barbiturates are frequently used with suicidal intent. A 25 per cent solution of pyridine betacarbonic acid diethylamide, in doses of 5 cc., was given intravenously to eighty-four male patients with psychosis who had been given sodium amytal, phenobarbital, ortal sodium or pentobarbital sodium in varying amounts, to study the effect of this drug on the narcosis produced with barbiturates. The same number of subjects were used as controls. Hiccup, which lasted from five to fifteen minutes, was noted in twenty-one cases after the administration of the drug. Five patients suffered from projectile vomiting after injection of 10 cc. of the drug. These reactions were not considered contraindications to the use of the drug. It is concluded that this is a good drug for the counteraction of extreme narcosis caused by the barbiturates.

Krinsky, Boston.

Vascular Action of a Mixture of Scopolamine and Chloralose. H. Baruk, Gevaudan, R. Cornu and J. Mathey, Ann. méd.-psychol. **94**:187 (July) 1936.

In a series of previous reports Baruk discussed the remarkable therapeutic action of a mixture of scoplamine and chloralose (scopochloralose) in hysteria. The preparation lowers the systolic pressure; this is its most constant effect. The differential and the diastolic pressures are much less affected. However, in some instances the differential pressure shows a slight tendency to fall. The pulse rate nearly always slows but frequently becomes dicrotic. The changes in the oscillometric index are variable; sometimes the amplitude diminishes slightly; this is often striking in hypertensive patients with unstable vascular systems and a high oscillometric index. Sometimes the index is increased, especially in subjects with a low index, as though the drug had a regulatory effect on the vasomotor system. The intensity of all these effects varies according to the dose of the drug, but they are observed even when small doses are used. The reaction reaches its maximum about one and a half hours after the administration of the drug and rapidly decreases thereafter. The vasomotor system in hysterical persons is abnormally labile. The preparation of scopolamine and chloralose diminishes vascular irritability through its inhibitory action on the cerebral cortex, with a resulting sedative effect on the vasomotor system.

Yakovlev, Waltham, Mass.

Corneal Lesions Following Removal of the Gasserian Ganglion for Trigeminal Neuralgia. C. Drutter, Deutsche Ztschr. f. Chir. **248**:55 (Dec. 9) 1936.

Drutter reports that of sixty-nine patients treated by injection of alcohol into the gasserian ganglion for the cure of trigeminal neuritis seventeen (24.6 per cent) had keratitis. In nine (52.9 per cent) the lesion remained permanent. Eighteen patients were subjected to twenty-seven operations for the removal of the gasserian ganglion. The cornea remained normal in all cases. The author concludes that neuroparalytic keratitis develops only as a result of anesthesia of the cornea. The cause of keratitis remains unexplained in spite of many studies. Primary trigeminal neuralgia seldom involves the first branch of the nerve. Pains in this area are considered secondary by many authors. The incidence of corneal anesthesia and consequent disease of the cornea cannot be diminished through the use of the method developed in Germany of injecting alcohol into the gasserian ganglion. The subtotal section of the posterior ganglion of the root of the trigeminus nerve, according to the method of Frazier and Spiller, does not lead to loss of sensitiveness of the cornea and to neuroparalytic keratitis. The persistence of high mortality in Germany following the operative intervention is due to lack of experience. The treatment with injection of alcohol makes the operative

intervention even more difficult. The operative method of subtotal section has a smaller percentage of recurrences than that of injection of alcohol. According to American authors, subtotal resection of the posterior ganglion is the method of choice in the treatment of trigeminal neuralgia. The author suggests that the injection method should be reserved for patients whose general condition will not justify a major procedure. Younger patients should be treated as far as possible by operative intervention, so as to avoid the possibility of keratitis.

EDITOR'S ABSTRACT. [J. A. M. A.]

Muscular System

CONGENITAL MUSCULAR HYPERTROPHY. B. E. HALL, F. W. SUNDERMAN and J. C. GITTINGS, Am. J. Dis. Child. **52**:773 (Oct.) 1936.

The authors describe the case of a male Negro infant who exhibited generalized muscular hypertrophy with greater than normal strength, mental deficiency and extrapyramidal motor disturbances manifested by hypertonia, slight resistance to passive movement, slight rigidity of the neck and a tendency to assume the position of opisthotonos. The features last mentioned tended to disappear in a few months. Specimens taken for biopsy and the electrical reactions of the muscle were normal. There was abnormally high excretion of creatine and creatinine in the urine. The concentrations of potassium, inorganic phosphate and phosphatase in the blood serum were increased. Roentgenograms of the skull, abdomen and renal pelves were normal. Examination of the spinal fluid gave normal results. Bruck and DeLange reported cases of the same syndrome in which necropsy was performed. The brain of Bruck's patient was reported as normal, and that of DeLange's as showing malformation of the corpus striatum and widespread porencephaly.

WAGGONER, Ann Arbor, Mich.

PATHOGENESIS AND TREATMENT OF MYOTONIA CONGENITA. H. G. PONCHER and H. WOODWARD, Am. J. Dis. Child. **52**:1065 (Nov.) 1936.

An infant with myotonia congenita was studied carefully for three years. Examination showed: enlargement of the tongue; uniform, generalized muscular hypertrophy; sustained contraction of a muscle on percussion, and altered response of the muscle on galvanic stimulation; i. e., on one occasion the cathodal closure contraction was less than the anodal closure contraction, and on another they were equal. A specimen of the gastrocnemius muscle taken for biopsy showed normal size and structure of the fibrils. When the infant was excited or made uncomfortable, there were myotonic attacks, characterized by cyanosis, opening the mouth, hyperextension of the lower limbs and gasping respirations, followed by complete relaxation and return to a normal color.

The physiologic creatinuria of infancy was absent, but on administration of thyroid substance creatine was excreted and the myotonic symptoms disappeared. A decrease in the amount of creatine excreted was invariably associated with myotonia. Infection, such as measles and whooping cough, caused decreased creatinuria and a return of myotonia, although the myotonic symptoms could be relieved by an increase in the dose of thyroid.

An adult patient with myotonia congenita was fed thyroid substance, but his response was different from that of the infant. In the adult there was induced neither creatinuria nor relief from myotonia but rather accentuation of the myotonic symptoms.

WAGGONER, Ann Arbor, Mich.

MYASTHENIA GRAVIS IN CHILDREN: ITS FAMILIAL INCIDENCE. H. B. ROTHBART, J. A. M. A. **108**:715 (Feb. 27) 1937.

Rothbart discusses two cases of myasthenia occurring in brothers, in whom the onset was in early infancy. There are two, possibly three, other cases of myas-

thenia gravis in the family, suggesting heredity as an important etiologic factor. Three of five siblings were affected in varying degree, all in early infancy. One other child probably had the disease, but in a mild form, presenting only lagophthalmos; he recovered completely, but with a tendency toward recurrence during any acute illness. All the patients were boys. One sister in the family is healthy and shows no evidence of weakness. In the first case improvement was entirely due to the combined action of amino-acetic acid and ephedrine. There is still considerable weakness with little change in the facial weakness, ophthalmoplegia or lagophthalmos, although the patient is able to keep his eyes open fairly wide for several hours in the morning. In the past year little improvement has taken place, but with cessation of the medication he immediately becomes worse. Infections of the upper respiratory tract have been rather frequent, and these incite a relapse. When first seen in 1930 the "asthmatic" attacks were considered to be of allergic origin. The author now recognizes that the asthmatic spells were due to fatigability of the muscles of respiration. Laboratory studies have not revealed anything of significance except increased creatinuria. The thymus gland, often observed to be enlarged in such cases, was normal. The long bones presented changes usually identified with pseudohypertrophic muscular dystrophy, which account for the peculiar waddling gait seen in both diseases. It is possible that coxa valga is the result of weakening of the muscles and ligamentous supports of the joints. In the second case spontaneous improvement occurred without the aid of any medication or other kind of therapy. So far this boy has had no relapse, although his recovery cannot be said to be complete, in view of the persisting ophthalmoplegia and residual postoperative lagophthalmos. It would be hazardous to state that a relapse may not occur, since recurrences have been observed even after many years of apparent cure, mostly in adults. EDITOR'S ABSTRACT.

OCCUPATIONAL SPASM. C. I. URECHIA, L. DRAGOMIR and M. RETEZEANU, Arch. internat. de neurol. **54**:407 (Oct.) 1936.

Three cases of occupational spasm in which excessive use of the involved muscles seemed to be a factor are reported by Urechia and his associates. In two patients the feet were involved. One of these was a street-car conductor who had to remain on his feet all day. His attacks consisted of contractions of the right gastrocnemius muscle, with flexion at the knee and ankle. Studies of the blood revealed increase in calcium and diminution in phosphorus. A Chvostek sign was elicited, suggesting a possible parathyroid factor. The second patient with involvement of the leg had to carry heavy sacks on his back, throwing most of his weight on the right foot. Cramps developed in the toes, with pain radiating to the popliteal fossa and flexion of the feet. The third patient a mechanic, experienced painful cramps in the right arm, lasting for from thirty to forty seconds, producing flexion at the elbow. The condition was aggravated by fatigue and improved by rest. Although in this patient there was diminution in the phosphorus content of the blood, the calcium was normal. The authors believe that a physiologic element, associated with rest, use and muscle metabolism is at least as important as the emotional element in cases of occupational spasm.

DAVIDSON, Newark, N. J.

PATHOLOGIC OBSERVATIONS IN MYASTHENIA GRAVIS. J. SCHEINKER, Monatschr. f. Psychiat. u. Neurol. **93**:111 (April) 1936.

In a clinically typical case of myasthenia gravis, necropsy disclosed a tumor of the thymus. Microscopically, the tumor consisted of lymphoid and epithelioid cells. Numerous collections of round cells were observed in the skeletal muscles, chiefly in the perimysium internum. In the medulla and pons the walls of the smaller vessels were infiltrated with lymphoid and epithelioid cells which resembled the cells encountered in the tumor. The vessels themselves were not otherwise altered, and neuroglial changes could not be demonstrated. No alterations were

observed in other parts of the nervous system. Scheinker points out that in several recently reported cases of myasthenia gravis perivascular infiltrations have been noted in the central nervous system and elsewhere. These infiltrations have generally been regarded as inflammatory phenomena, but this interpretation is not justified in the present case, in view of the lack of neuroglial reaction and the absence of alterations in the walls of the vessels. Scheinker raises the question whether the infiltrations observed by him in the vessels of the medulla and pons may be metastases from the tumor in the thymus. The presence of epithelioid elements in these cellular accumulations and the absence of surrounding inflammatory phenomena in the nervous tissue lend support to such a supposition.

ROTHSCHILD, Foxborough, Mass.

Special Senses

KINETIC TEST FOR STEREOSCOPIC VISION. F. H. VERHOEFF, Arch. Ophth. **15**:833 (May) 1936.

In previous articles Verhoeff described two tests which when the results are positive are the only conclusive tests for stereoscopic vision which have been presented. These two tests require fairly high visual acuity. Moreover, with any form of subjective test, as Verhoeff points out, there is a certain degree of probability, when the results are negative, that consciousness has rejected the information sent to it. Verhoeff devised the tests presented for stereoscopic vision, the effect of depth being so marked that the probability of the stereoscopic information being rejected is reduced to a minimum and the test can be employed successfully when the visual acuity in one or both eyes is as low as 10/200.

The new test introduces three features which have never previously been employed for testing the perception of depth: (*a*) the perception of motion forward and backward due to motion of a retinal image in one eye only; (2) the utilization of strong monocular perspective to prevent conflict between monocular and binocular information, and (3) the utilization of replacement, dependent on high attention value, to identify a retinal image that is apparently moving but is actually stationary. Verhoeff describes in detail the cards which he uses in an ordinary Brewster stereoscope and the technic of the test.

Hitherto the only evidence that change in convergence is not essential to the stereoscopic perception of depth has been the observation that stereopsis is possible with momentary excitation of the retinas. A slight modification of Verhoeff's test presents new and more satisfactory evidence of this. Under these conditions it is evident that the stereopsis obtained is due not to changes in convergence but to changing disparateness of the retinal images of the two slides viewed. Moreover, since the effect of depth is about the same whether or not convergence is allowed, it follows that change in convergence does not play an important role, even in estimating the amount of depth determined by stereopsis. Another phenomenon that can be studied is delay in binocular fixation. Verhoeff found that exact binocular fixation is achieved less rapidly by relative divergence, or abduction, than by convergence, or adduction.

When the test cards are used in the amblyoscope, convergence of the amblyoscopic tubes causes the fused image to appear as though it approached the examiner and to become smaller and, at the same time, relatively shorter. When the tubes are diverged, the fused image appears to recede and become larger and, at the same time, relatively longer. These observations demonstrate the relation of apparent size and apparent distance; in addition, they show that the effect of a given disparateness is a function of the apparent distance of the point of binocular fixation. It should not be assumed that these observations are determined by the amount of convergence, since the possibilities that it is determined by changing disparateness or by delay in binocular fixation are not excluded.

SPAETH, Philadelphia.

TWINNING AND OCULAR PATHOLOGY, WITH A REPORT OF BILATERAL MACULAR COLOBOMA IN MONOZYGOTIC TWINS. ARNOLD GESELL and EUGENE M. BLAKE, Arch. Ophth. **15**:1050 (June) 1936.

Gesell and Blake report a case of bilateral macular coloboma, which is a rare congenital anomaly. The occurrence of four remarkably similar colobomas in the four eyes of a pair of twins is especially noteworthy. Apart from their significance for ocular pathology, the cases reported furnish a remarkable instance of exquisitely detailed concordance in monozygotic twins. Comparative studies of 453 pairs of monozygotic and dizygotic twins culled from the literature are included.

SPAETH, Philadelphia.

BLINDNESS CAUSED BY ACETYLARSAN. J. CHARAMIS, Ann. d'ocul. **172**:314 (April) 1935.

Charamis reports the case of an elderly patient with syphilis associated with cardiorenal disturbance, in whom total blindness (toxic optic neuritis followed by bilateral papillary atrophy) was produced by acetylarsan (the parahydroxacetylaminophenylarsinate of diethylamine). The symptoms were manifested after injection of 3 cc. of the drug, and blindness occurred after the injection of 9 cc. The ocular lesions were probably caused by a cardiorenal condition, which aggravated the toxic neuritis.

Dupuy-Dutemps observed that the toxic action of pentavalent arsenic preparations on the optic nerve, although rare, must be considered. He urged discretion in their use, unless their superiority over other preparations is unquestioned. Terrien reported the case of a nonsyphilitic patient who after receiving five injections of acetylarsan acquired retrobulbar neuritis resulting in marked reduction in visual acuity in spite of treatment with sodium thiosulfate. Hartmann stated that the indications for the use of pentavalent arsenic preparations must be carefully observed. In the Lariboisière Hospital there has been no ocular accident since acetylarsan has been used, that is, for the past six years. During this period 1,067 patients received 20,400 injections.

BERENS, New York.

SPASM OF THE RETINAL ARTERIES. P. BAILLIART, SCHIFF-WERTHEIMER and A. ROLLIN, Ann. d'ocul. **172**:1015 (Dec.) 1935.

Bailliart, Schiff-Wertheimer and Rollin report the case of a patient aged 59 who had peripheral blindness, with conservation of central vision. Examination during an attack revealed paleness of the optic disk, and filiform stricture of the arteries in the form of beads. Tension in the retinal arteries was 100 mm. Retinal edema was present. Vision in each eye was 10/10. After a series of twenty injections of acetylcholine, the patient's general condition improved. The optic disks are still pale, but the maculae are normal.

BERENS, New York.

SUBJECTIVE OCULAR DISTURBANCES FOLLOWING CRANIAL TRAUMATISM. AUBINEAU, Ann. d'ocul. **173**:205 (March) 1936.

Aubineau reports twenty-one cases of cranial traumatism, caused usually by automobile accidents, followed by more or less prolonged loss of consciousness. These injuries produced certain objective ocular manifestations, either sensorial (affecting the optic nerve in one case) or paretic (isolated paralysis and paralysis of associated movements in two cases each); all produced the same subjective ocular disturbance. These subjective ocular disturbances may be divided into two groups: (1) those consisting of definite visual disturbance and (2) those consisting of asthenopic disturbances.

1. The first group may be produced by various causes (i. e., physical exertion, lowering of the head or sudden shock, which may be insignificant, resulting from atmospheric changes); they are associated with vertigo; the patient has the

sensation of falling and reaches for support, without falling, however, without turning or lateral movement, without nausea and sweats, as in true vertigo, and without moments of unconsciousness, as in indefinite epileptic manifestations. Complete blindness, such as sector defects in the visual field which are caused by angiospasm, scintillating scotoma or scotoma occurring in ophthalmic migraine, does not occur; there is no rapid reduction of visual acuity similar to that which characterizes blindness caused by intracranial hypertension (i. e., choked disk). The patient is unable to fix objects, and there is marked displacement of images, which begins and ceases suddenly as the sensation of dizziness occurs. The duration of these attacks is short, and their frequency is variable.

2. Asthenopic disturbances affect the use of the eyes and the voluntary fixation of objects; they consist of more or less rapid "ocular fatigue." This type of asthenopia is independent of normal accommodation, cannot be corrected by lenses and is independent of normal ocular muscle balance. Accommodative and convergence asthenopia may also exist. The patient may have disturbance of visual fixation, inability to use his eyes and asthenopic ptosis. Although the patient's ability to fix objects is disturbed, vision and visual function are not affected; after a variable length of time the patient is usually forced to discontinue using his eyes.

In summarizing, Aubineau states that all patients with cranial injuries should receive a thorough neuro-ocular examination. All craniocerebral injuries may present objective and subjective ocular manifestations. Subjective ocular disturbances, identical with psychoneurotic disorders, seem to be associated with cranial injuries; these disturbances have an indefinite, but true, organic basis, which influences the prognosis. From the medicolegal point of view, ocular signs lead to a definite diagnosis of ocular disease. Subjective ocular disturbances, on the contrary, should be considered with the "concussion syndrome," of which they are a manifestation.

BERENS, New York.

SPASM OF CONVERGENCE ASSOCIATED WITH STRABISMUS AND TRANSITORY DIPLOPIA. BAILLIART, Ann. d'ocul. **173**:220 (March) 1936.

Bailliart reports the case of a girl aged 7 years who had three attacks of transitory diplopia associated with strabismus. During the last attack there was muscular deviation of approximately 40 degrees. However, if the patient's attention was diverted, the eyes no longer deviated. The three attacks were preceded either by shock or by slight injury. There was nothing significant in the previous findings. Procaine hydrochloride injected into the right medial muscle arrested the spasm of the muscle; after this treatment strabismus has not been present. However, from time to time the patient closes one eye while using her eyes, which caused Bailliart to believe that she may have slight diplopia.

BERENS, New York.

FUNCTIONAL EXAMINATION OF THE KIDNEYS IN RELATION TO OPHTHALMIC FINDINGS. A. DUBOIS-POULSEN, Ann. d'ocul. **173**:381 (May) 1936.

According to Dubois-Poulsen, some authorities believe that there is an almost constant parallelism between the existence of exudative retinal processes and lesions of the kidney. They assert that retinitis indicates nephritis in all cases in which white plaques are present in the retina, particularly in diabetic retinitis. However, de Wecker, Dianoux and Morax expressed the belief that the presence of nephritis in a diabetic patient produces retinitis. Beauvieux and Pesme showed that the anatomicopathologic lesions of albuminuric retinitis and diabetic retinitis are identical. Many have stated that retinitis appears only in the presence of renal deficiency. Numerous disagreements have arisen in clinical studies. For specific and general reasons, the duality of the two diseases have been accepted by numerous authors. However, functional studies should solve this problem.

Onfray presented the following classification, which is an aid in differential diagnosis: Of twenty diabetic patients with retinitis, he observed azotemia, below

0.5 Gm. in ten patients, between 0.5 and 0.7 Gm. in four, between 0.7 and 0.9 Gm. in three and of 1 Gm. or more in three. Ambard's constant was normal in 25 per cent of the patients, slightly elevated (between 0.9 and 0.11) in 18 per cent and low in 57 per cent. Therefore, it is evident that the renal lesion is a frequent, but not a constant, complication. Even though no pathogenic deduction can be made from these facts, the clinical frequency of renal disturbances and their prognostic interest for diabetic patients with ocular lesions must be acknowledged. Dubois-Poulsen believes that more thorough studies undertaken in the light of new methods of functional examinations would be valuable.

BERENS, New York.

STUDIES ON THE VISUAL AND AUDITORY PATHS: I. COMMISSURE OF GUDDEN. P. QUERCY and R. DE LACHAUD, Encéphale **31**:61, 1936.

The pathways of vision and audition are widely separated at their origins and terminations, but the middle portions of the two paths, namely, the colliculi, the geniculate bodies and the optic tracts, are close together. This may have some relation to intersensory connections and particularly to synesthesia. For this reason, Quercy and de Lachaud studied the commissure of Gudden. Gudden concluded that the portion of the optic tracts and posterior border of the chiasm which remains after enucleation of the eye in animals constitutes a commissure and is independent of the optic pathway. Gudden, however, observed that the optic nerves do not disappear entirely after enucleation. "He seemed to forget that the optic tract does not disappear, any more than the optic nerve; he insisted that it disappeared entirely. One may ask whether it is not a remnant of the tract which constitutes the commissure to which his name has been given." Other observers, such as Dejerine, maintained that after enucleation the entire chiasm and tract degenerate, including the commissure of Gudden. Quercy and de Lachaud studied these structures in the rabbit, mole and man. The commissure of Gudden could not be distinguished grossly in any of the species. In the rabbit an apparently transverse bundle of fibers seen microscopically at the posterior part of the middle level of the chiasm was shown in serial sections to be constituted of intercrossing fibers coming from an upper or a lower level. The termination of the optic tract by subdivision into two parts, one for each geniculate body, seems grossly apparent in man, but serial sections showed that the entire optic tract ends in the lateral geniculate body. These two structures are closely connected and are everywhere separated from the medial geniculate body by a septum of tissue rich in nerve elements and of complex texture, which is worthy of separate study.

LIBER, New York.

CLINICAL AND INSTRUMENTAL VESTIBULAR REACTIONS IN A CASE OF UNILATERAL ACUTE LABYRINTHITIS, FOLLOWING SLIGHT ACUTE OTITIS. J. A. BARRÉ and A. CHARBONNEL, Rev. d'oto-neuro-opht. **14**:246 (April) 1936.

Labyrinthitis following acute otitis is rare. The case is reported of a girl aged 17 years, who after acute catarrhal otitis on the left side suddenly became dizzy, with nystagmus to the right, vomiting and tinnitus. The symptoms lasted two days and were then relieved by vigorous blowing of the nose, only to return two days later, accompanied by slight fever. Warm and cold caloric tests on the diseased ear produced no reaction; the tests on the sound ear which should have reversed or annihilated the preexisting vestibular syndrome were without effect, while those that acted in the direction of the spontaneous phenomena reenforced them strongly. The various excitations (rotatory, thermic and galvanic), when applied to the two ears therefore had only one effect: that of exaggerating the existing manifestations. Reexamination twenty-eight days later revealed no clinical signs of disturbance in vestibular function. Instrumental tests showed lack of reaction to the caloric test in the right ear and a slight reaction in the left. There was a subnormal response to rotation in both directions. The poor and partial responses to stimulation are

explained by assuming that the cure was not complete. Attention is called to the results of the experiments of Bauer and Leidler and others, who observed that in an animal with one cerebral hemisphere removed provoked nystagmus was more accentuated in one direction, whichever vestibule was stimulated.

DENNIS, San Diego, Calif.

EFFECTS OF SHORT WAVES OF HIGH FREQUENCY ON THE SUPERFICIAL CIRCULATION OF THE OCULAR GLOBE, THE RETINA AND THE OPTIC NERVES. CARLOTTI, JACQUET and ROLAND, Rev. d'oto-neuro-opht. **14**:260 (April) 1936.

Short waves of high frequency are usually applied in doses of from several hundred to 1,000 watts. In order to exclude the effects of elevation of temperature in the tissues, the authors employed a current of $\frac{1}{10}$ watt, and, owing to the high frequency, the patients received only $\frac{1}{10}$ of the current delivered by the apparatus. The applications were monopolar, the electrode being placed on the forehead or some indifferent part of the body, or even in not immediate contact. The effects of this current were observed on the superficial circulation of the ocular globe, the retinal circulation, the vascularization of the optic nerve and the tension of the ocular globes, fifteen normal and eleven pathologic eyes being studied. The effects on the tension of the globe were uncertain, and the influence on diminution of arterial tension in the retina was not clearly proved. Marked vasodilatation of the retinal vessels was obtained in about one minute and was maintained for from thirty-six to forty-eight hours in normal subjects. This action was produced more quickly and intensely and disappeared more rapidly in young persons. The current should not be applied in subjects with a tendency to local congestion. On the other hand, in patients with pathologically contracted retinal vessels useful results were obtained, both anatomically and clinically. These results seem to be lasting. The effects of the application of short waves should be studied in all ocular and cerebral spasmodic phenomena. Other treatment, such as pilocarpine for glaucoma and acetylcholine for retinal and cerebral spasms, should not be abandoned; the short waves enhance their action.

DENNIS, San Diego, Calif.

OTOVESTIBULAR STUDY OF TWENTY-SIX CASES OF CLOSED CRANIOCEREBRAL TRAUMATISM. M. MEULDERS and J. HELSMOORTEL JR., Rev. d'oto-neuro-opht. **14**:449 (July-Aug.) 1936.

It is as essential to make a complete vestibular examination in cases of trauma as to examine the auditory function. To the classic Bárány tests have been added tests of the otolithic apparatus described by Quix. Nystagmus itself has become complex. Quix has proved that it is caused by excitation of all the canals and not of one only and that it is the result of an ampullofugal or an ampullopetal endolymphatic current. Vertical, rotary or diagonal nystagmus is always of central origin; violent spontaneous nystagmus not accompanied by deviation of the arms is likewise of central origin. In peripheral disturbances nystagmus and deviation of the arms are in the same direction. (Evidently, the authors classify the direction of nystagmus by that of the slow component. Abstracter.) If nystagmus and deviation of the arms are in different directions, the origin is central. In the study of the present group of cases, special importance has been given to Quix' tests, especially the test for saccular sensibility, since the object sought here is the demonstration of a peripheral lesion.

Protocols in twenty-six cases are given. Otolithic disturbances were present in fourteen cases; hyperexcitability of the maculae was observed much oftener than paresis. Vestibular tests gave normal results in six cases, hypo-excitablity in nine and hyperexcitability in four; in five instances hypo-excitability was observed for certain tests and hyperexcitability for others. In three cases symptoms of disturbances of central origin were present. Great importance is attached to spontaneous deviation of the index finger (past pointing), the side affected

corresponding to the side of the lesion. Romberg's test gave positive results six times, and the sensitized Romberg test, four times. The caloric test was more sensitive than the rotatory. The galvanic test was useful on nine occasions in determining the territory involved.

DENNIS, San Diego, Calif.

INTERMITTENT DIPLOPIA, PRECEDING INVASION OF THE ORBIT BY A MUCOCELE OF THE FRONTAL SINUS. JEAN SÉDAN, Rev. d'oto-neuro-opht. **14**:561 (Sept.-Oct.) 1936.

Sédan discusses the curious fact that invasion of the orbit and displacement of its contents by a mucocele of the frontal sinus are frequently not accompanied by troublesome diplopia and the further fact that when diplopia has been present before rupture of the mucocele into the orbit, it frequently disappears after such rupture. An illustrative case is reported. The explanation for the second phenomenon is that the diplopia is caused by paresis of the superior muscles of the orbit, lying in contact with a focus of osteitis. It is more difficult to explain the first observation. A possible factor is that the displacement of the globe is more horizontal than downward. It is known that horizontal displacements may be considerable without giving rise to diplopia.

DENNIS, San Diego, Calif.

UNILATERAL ABSENCE OF PUPILLARY REACTION TO LIGHT FOLLOWING SEVERE HERPES ZOSTER IN THE AREA (INCLUDING THE CORNEA) SUPPLIED BY THE FIRST AND SECOND DIVISIONS OF THE TRIGEMINAL NERVE. J. ZUTT, Monatschr. f. Psychiat. u. Neurol. **93**:305 (Aug.) 1936.

A man aged 67 had herpes zoster of the right side of the face and was severely ill, with high fever and great pain. He was confined to bed for two months and thereafter sought medical aid because of pain in the right side of the face and head. Examination revealed redness and slight swelling of the skin of the right side of the face and head, partial loss of hair and keratitis herpetica on the right and a sluggish reaction of the right pupil to light. Several months later the area of skin supplied by the first and second divisions of the right trigeminal nerve displayed scarring, loss of pigment and yellow-brown fissures. In this area there was impairment of all forms of sensation, and the right corneal reflex was diminished. The right pupil failed to react to light on direct as well as consensual stimulation. The left pupil reacted promptly to light on direct stimulation and on stimulation of the right eye. Both pupils reacted well in convergence. There was inequality of the pupils, which varied according to the degree of illumination. Apart from these changes, neurologic examination disclosed essentially normal results, and the spinal fluid failed to show any changes characteristic of neurosyphilis. Zutt points out that several similar cases have been reported. The observations indicate that peripheral involvement may lead to the Argyll Robertson phenomenon. The lesion may be located in the ciliary ganglion or in the ganglionic elements scattered through the iris. In view of these observations, it is necessary to assume that in the peripheral motor part of the reflex arc impulses arising from light and those from convergence stimuli follow separate courses, as a result of which there may develop isolated disturbance of the reflex pathway for light.

ROTHSCHILD, Foxborough, Mass.

Basal Ganglia

SPEECH PRESERVATION AND ASTASIA-ABASIA FOLLOWING CARBON MONOXIDE INTOXICATION. L. H. COHEN, J. Neurol. & Psychopath. **17**:41 (July) 1936.

Cohen reports a case of carbon monoxide intoxication which was followed by a variety of neurologic and mental symptoms. The neurologic signs of masked facies, general flexor posture, tremor, poverty of movement and propulsive gait pointed to damage of the basal ganglia. Cerebral involvement was inferred from defects in attention, memory and associations and the picture of dementia. Of chief

interest were the perseverations of speech and writing and the astasia-abasia, which have previously been noted only in a case of carbon monoxide poisoning reported by Wolff. The close association between the perseveration and the tremor in their course and ultimate recovery suggests a similar localization in the basal ganglia. This is in agreement with the findings of Merzbach, who noted the relationship of perseveration and damage to the caudate nucleus. In consideration of the other disturbances in gait of an extrapyramidal nature, the astasia-abasia may have been due also to dysfunction of the basal ganglia, but undoubtedly this symptom also had a hysterical component. Cohen suggests that both the perseveration and the astasia-abasia may be explained on the basis of hypersuggestibility. It is not assumed that suggestibility is a specific function of the basal ganglia, but in damage to this area a lowered threshold (increased suggestibility) for the repetition of activities initiated from higher centers may be produced.

N. Malamud, Ann Arbor, Mich.

Disturbances of Hepatic Function in Diseases of the Striatum. K. Haug, Monatschr. f. Psychiat. u. Neurol. **89**:320 (Oct.) 1934.

Studies of the functional activity of the liver were made in eleven cases of disease of the corpus striatum. This group included four patients with paralysis agitans and five with postencephalitic parkinsonism. The methods used were the galactose tolerance test and the determination of urobilinogen in the urine. The first test disclosed impairment of function of the liver in eight cases, and the second, in ten cases. Scopolamine hydrobromide and atropine, which were given to some of the patients, influenced the neurologic symptoms favorably and improved the activity of the reticulo-endothelial system, but increased the disturbance of carbohydrate metabolism. On the other hand, decholin and paraldehyde failed to change the clinical condition, though the functional activity of the liver was improved by decholin and impaired by paraldehyde. It is evident from Haug's studies that amelioration of the disturbed functional activity of the liver cannot be expected to influence the neurologic alterations favorably. In the impairment of hepatic function observed by Haug, a leading role must be attributed to the cerebral changes, which involve certain centers controlling metabolism.

Rothschild, Foxborough, Mass.

Experimental Pathology

Growth of Rous Sarcoma Inoculated into the Brain. E. Vazquez-López, Am. J. Cancer **26**:29, 1936.

Intracerebral growth of the Rous sarcoma was produced both by implantation of tissue grafts and by injection of cell-free material (filtrates or desiccated extracts). When grafts are implanted, the tumor grows at the expense of the transplanted tissue, forming well limited nodules without invasion of the surrounding nerve tissue, which is compressed and displaced. When cell-free material is injected, the tumor grows diffusely, invading the brain by cellular infiltration, especially along the perivascular Virchow-Robin spaces. In the first stages of development the tumor is constituted of accumulations of compound granular corpuscles derived from microglia cells and similar to those commonly produced in all pathologic processes of the nerve parenchyma. Later the tumor cells appear among these elements. The tumor evokes a strong neuroglial reaction in all the surrounding area. The microglia cells react by migration and accumulation throughout the periphery of the neoplasm. This response is more conspicuous in tumors produced by cell-free material. There are morphologic, topographic and tinctorial relations between the microglial cells and their derivatives, on the one hand, and the ameboid elements of the Rous sarcoma, on the other, which force the conclusion that they are identical. The fact that the tumor develops in its early stages at the expense of the compound granular corpuscles (derived from microglial cells) and the relations of the microglia to the ameboid cells of the

tumor compel one to suppose that the microglial response, at least in the advanced stages, probably is not defensive but is provoked by a stimulus arising from the free sarcoma agent, which acts always on cells with characters similar to those of the microglia cells. FROM THE AUTHOR'S SUMMARY. [ARCH. PATH.]

ON THE EXISTENCE OF AN INTRINSIC DEFICIENCY IN PELLAGRA. V. P. SYDENSTRICKER, E. S. ARMSTRONG, C. J. DERRICK and P. S. KEMP, Am. J. M. Sc. **192**:1 (July) 1936.

In view of the work of Castle and his associates on pernicious anemia, it was determined to test the efficacy of the normal gastric juice as a source of a hypothetic intrinsic factor in pellagra. Six patients were treated with gastric juice in varying amounts for from ten to forty-nine days. All patients but one were fed a pellagra-producing diet. Three patients with severe pellagra improved more rapidly than was expected, even when the optimum diet fortified with vitamin B_2 was administered. It is suggested that an intrinsic factor is present in normal gastric juice which makes possible the utilization of minimal amounts of the extrinsic factor (vitamin B_2). Prolonged remission in two instances indicates that this factor may be stored in the body and that there may be in pellagra an intrinsic deficiency of variable degree. The intrinsic factor is exhausted or cannot be regenerated during prolonged deprivation of the extrinsic factor.

MICHAELS, Boston.

INTRACEREBRAL INOCULATION OF FETAL GUINEA PIGS WITH BACILLI CALMETTE-GUÉRIN AND THE H_{37} STRAIN OF THE TUBERCLE BACILLUS. I. S. NEIMAN and O. C. WOOLPERT, Am. J. Path. **12**:153, 1936.

Guinea-pig fetuses were inoculated with graded doses of BCG and the effects compared with those obtained in a similar series inoculated with virulent tubercle bacilli (H_{37}). Both types of tubercle bacilli were found to spread from the site of inoculation, but not with equal rapidity; with the same dose, it took a longer time for BCG to cause as much pathologic change in the animal as a whole as did H_{37}. Pathologically the response of the fetus to the two organisms was the same. Histologic evidence is brought forward to show that BCG is capable of multiplying the fetal tissues and of initiating a disease process different only in degree from that produced by H_{37}. So far, attempts at fetus to fetus transfer of BCG have not been successful. Recovery of this bacillus from inoculated fetuses by cultivation on artificial mediums was accomplished four times in twenty-four attempts.

FROM THE AUTHORS' SUMMARY. [ARCH. PATH.]

THE EFFECTS OF A HIGH FAT DIET, OF INANITION, OF THE INJECTION OF ACETONE ALONE OR WITH FLUIDS OF VARYING OSMOTIC PRESSURE UPON EXPERIMENTAL CONVULSIONS IN CATS. SARAH R. RIEDMAN, Bull. Neurol. Inst. New York **4**:624, 1936.

This study was suggested by the widespread use of the ketogenic diet in the treatment of epilepsy. The problems of ketogenic diet, fasting and the possible dehydration resulting therefrom are reviewed briefly. Not much importance is given to the blood sugar, the protein metabolites or the calcium and phosphorus of the blood as factors responsible for the improvement of epilepsy with ketosis; attention is centered rather on acidosis as manifested by the lowered alkali reserve and change of p_H, loss of fixed base and dehydration.

Convulsions were induced by the injection of absinth or by electrical excitation of the cerebral cortex in fasting cats and in cats kept on a ketogenic diet. In both groups the susceptibility to convulsions, produced by injections of absinth, was increased. The intravenous injection of acetone resulted in a definite rise in the minimal convulsive dose of absinth. Injection of tap water produced a slight decrease in the minimal convulsive dose. Injections of equimolecular, isotonic solutions of dextrose had no effect on the results produced by acetone, but

a 25 per cent solution of dextrose raised the minimal convulsive dose still more. Injections of acetone also decreased the severity of the convulsions caused by electrical stimulation and sometimes prevented them completely for several successive excitations.

Fasting cats showed a greater susceptibility to the production of convulsions than cats used as controls, in spite of ketosis. The production of abnormal hydration, due to partial protein starvation, possibly is an important factor in causing convulsions.

In view of the effect of acetone, it is difficult to explain the variation and frequent ineffectiveness of the ketogenic diet in the clinical field. The suggestion is made that, while the ketosis is effective in raising the convulsive threshold, there are other effects of the diet as yet unknown which may operate in the opposite direction.

KUBITSCHEK, St. Louis.

THE EFFECTS OF LESIONS OF THE DORSAL COLUMN NUCLEI IN THE MACACUS RHESUS. A. FERRARO and E. BARRERA, Brain **59**:76, 1936.

This communication is a sequel to the observations reported by the authors (1934 and 1935) on the effects of section of the dorsal columns and the restiform body. A review of the literature reveals relatively few reports dealing with the effects of lesions of the gracile and cuneate nuclei. Bechterew (1890) noted severe disturbance of equilibrium in dogs. Ferrier and Turner (1894) reported that when the nucleus gracilis, or clavate nucleus, of one side was destroyed, the animal showed a tendency to fall backward to either side; there was considerable swaying on exertion, and in walking the limb movements were slightly sprawling. Monkeys were used in this experiment. There was complete retention of the sensibilities of touch, pain and localization. Mott (1895) in monkeys cut the afferent fibers on one side as they leave the gracile and cuneate nuclei. He stated that there were inability to use the ipsilateral limbs and diminution of sensation on the side of the lesion. Tschermak (1898) destroyed the dorsal column nuclei on one side in cats. He expressed the belief that most of the symptoms he observed could be accounted for by disturbance of the sense of position and movement of the limbs. Probst (1902) reported on the effects of lesions of the dorsal column nuclei in dogs and cats. He compared the effects of such lesions with those resulting from lesions of the cerebellum. Mussen (1927), reporting on experiments in cats in which the nuclei graciles and nuclei cuneati were cauterized, claimed that the characteristic symptom was loss of postural sense involving the joints of one or more limbs.

Ferraro and Barrera used twenty-one Macacus rhesus monkeys in their investigation. The operations consisted of unilateral or bilateral destruction of the gracile and cuneate nuclei and unilateral destruction of the nucleus gracilis or of the nucleus cuneatus.

The symptoms which occur after bilateral lesion of the gracile and cuneate nuclei are mainly loss of sense of position in all extremities, hypotonia and transient loss or diminution of the hopping and placing reflexes. There are no appreciable changes in superficial sensibility. The deep reflexes are active. If the lesion involves the nucleus gracilis bilaterally, these symptoms are limited to both hindlegs, or to the ipsilateral leg, if the lesion is unilateral. If the lesion is restricted to the nucleus caneatus bilaterally, the symptoms are limited to the upper extremities, or to the ipsilateral upper extremity, if the lesion is unilateral.

The disturbances in the upper limbs resulting from lesions of the nuclei cuneati are more pronounced than those in the lower limbs following lesions of the nuclei graciles. Experiments on the dorsal columns and the cerebellum show that the nucleus of Clarke and Monakow, or the external cuneate nucleus, receives a large number of fibers from the funiculus cuneatus and that it sends fibers to the cerebellum by way of the restiform body of the same side. This nucleus, therefore, forms an intermediate station between fibers of the funiculus cuneatus and the cerebellum; it receives many of the impulses from the muscles of the upper limb and neck which ultimately go to the cerebellum. The medial cuneate nucleus,

or the nucleus cuneatus proper, receives fibers from the funiculus cuneatus and in turn sends arcuate fibers to the medial leminiscus and the thalamus, carrying impulses which ultimately will be associated with conscious deep sensibility. The fibers from the lower extremities terminate in the nucleus gracilis, which sends its efferent fibers into the leminiscus. A lesion of the nucleus gracilis, therefore, involves no appreciable cerebellar connection of the hindleg, and the disability resulting is dependent practically entirely on loss of the medullothalamic component. On the other hand, in a lesion of the nucleus cuneatus, especially when the lesion extends far enough laterally to involve the nucleus of Clarke and Monakow directly or the fibers from the nucleus cuneatus which pass into this nucleus, symptoms result not only from involvement of the fibers going to the contralateral cerebral cortex but from loss of impulses to the ipsilateral side of the cerebellum.

The symptoms resulting from lesions of the nuclei graciles and nuclei cuneati are similar to those following destruction of the posterior columns at high cervical levels. The intensity of the symptoms is more pronounced when the posterior columns are completely destroyed. This is due to the fact that in lesions of the poterior columns at the cervical level the cerebellar component which passes through the external cuneate nucleus is also destroyed. The symptoms resulting from lesions of the nuclei graciles and nuclei cuneati are similar to those which follow removal of the postcentral convolutions, but the latter are less pronounced, since the medial leminiscus sends impulses not only to the postcentral but to the precentral and parietal cortex.

SALL, Philadelphia.

INFECTION OF MONKEYS (MACACA MULATA) AND GUINEA-PIGS WITH THE VIRUS OF EQUINE ENCEPHALOMYELITIS. E. W. HURST, J. Path. & Bact. **42**:271, 1936.

The infection of guinea-pigs or rhesus monkeys with the virus of equine encephalomyelitis may be divided into the visceral and the nervous phase. In the guinea-pig the two phases tend to overlap; in the monkey they tend to be separated by an interval of several days. The nervous phase succeeds the visceral much less constantly in the monkey than in the guinea-pig. During the visceral phase virus circulates in the blood in greater amount than can be accounted for readily by its titer in the viscera, while at a site of inoculation in muscle little or no multiplication takes place and in the dermis only moderate local increase. It seems, therefore, that the virus must multiply chiefly either in the blood or in some tissue intimately connected with the blood stream and forming only a small part by weight of the various viscera. In the monkey, infection of the nervous system occurs at a time when the very prompt antibody response to the visceral infection is as complete as it ever will be; monkeys recovered from the visceral infection without obvious nerve involvement are not usually immune to intracerebral inoculation of fresh virus. On the other hand, guinea-pigs recovered without having shown nervous symptoms are immune to subsequent intracerebral inoculation. Unlike many neurotropic viruses, the virus of equine encephalomyelitis inoculated intramuscularly or intradermally does not reach the central nervous system by way of the local peripheral nerves. In many cases the changes suggest that the nervous system is infected with virus which during the period of circulation in the blood passed out on to the nasal mucosa and thence by the perineural lymphatics of the olfactory nerve to the subdural space. The evidence presented does not finally exclude a slow "growth through" the hemato-encephalic barrier as an alternative method of infection of the central nervous system, but in the monkey the virus does not pass directly from the blood into the cerebrospinal fluid. An argument is advanced to show the probable close resemblance of the virus of equine encephalomyelitis to certain other viruses capable of exciting nervous disease, viz., those of vesicular stomatitis, yellow fever and louping ill. As a group these viruses probably have "pantropic" affinities, but as they differ materially in their cellular affinities and mode of action from such pantropic viruses as pseudorabies, B virus and herpes, they must be relegated to a separate group.

FROM THE AUTHOR'S CONCLUSIONS. [ARCH. PATH.]

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Regular Meeting, April 13, 1937

A. A. Brill, M.D., *President, in the Chair*

Anterior Neuropathy in Diabetes. Dr. Jerome E. Alderman (by invitation).

Sections of the spinal cord of a patient with diabetes associated with flaccid paralysis of the lower extremities were studied. Grossly, the cord was shrunken and rubbery. Microscopically, the cells of the anterior horns were severely damaged or completely replaced by fat. The anterior nerve roots and the peripheral nerves of the cauda equina displayed marked degenerative changes. The blood vessels revealed a moderate amount of arteriosclerosis, with some fatty degeneration within their walls. This was most evident within the gray matter of the cord. Thus, the pathologic condition involved an almost selective attack on the anterior horn cells, and for this reason the term neuronopathy seemed especially appropriate.

Authors have expressed the belief that diabetic neuronopathy is caused by a toxic agent produced during the course of the diabetes.

Transitional Glioma. Dr. Grant Levin.

The case illustrates the features of a type of intracranial tumor called transitional glioma. The history extended over two months, beginning with dizziness, followed by anomia, hemiparesis, aphonia, incontinence and coma. Physical manifestations included conjugate deviation, hemiparesis, abnormal reflexes, cerebrospinal hypertension and pleocytosis, with an elevated protein content of the cerebrospinal fluid.

The patient died within twenty-four hours after admission to the hospital; postmortem examination revealed a firm, pinkish tumor, hemorrhagic in spots, which occupied the parietal, temporal and occipital lobes on the left and the septum pellucidum. Histologically, the tumor was infiltrating and cellular. The cells were fairly uniform in size and contained moderately chromatic, elongated nuclei. They displayed a slight tendency to palisade formation, but were otherwise without pattern. The endothelium of the numerous vessels was hyperplastic. A few small syncytial giant cells were present. Special stains revealed varying degrees of differentiation among the constituent glial elements of the tumor. Generally, the maturity of the cells was greater than that of spongioblasts, but fell short of that of fully ripe glia cells.

Globus (*Ztschr. f. d. ges. Neurol. u. Psychiat.* **134**:325, 1931) described a group of cases of glial tumor in which biopsies were repeated at intervals and autopsies were performed. He observed a progressive increase in malignancy as indexed by the degree of cellular differentiation and expressed the belief that the explanation lay in the overgrowth of the more mature cells by "germinal centers" of unripe cells. The tumor reported on here is offered as one which falls midway in the series of transitional forms between the completely undifferentiated spongioblastoma multiforme and the completely differentiated astrocytic, ependymal or oligodendroglial glioma.

DISCUSSION ON PAPERS BY DRS. ALDERMAN AND LEVIN

Dr. Israel Strauss: I wish to discuss first the presentation by Dr. Alderman. Clinically one frequently sees cases of diabetes in which the reflexes, especially

of the lower extremities, are either depressed or absent, and it is often said that this is due to neuritis. One also frequently encounters cases in which there is weakness in the extremities, sometimes with and sometimes without pain and occasionally with certain sensory disturbances which are not well defined, and one often designates the condition as peripheral neuritis due to diabetes. In instances in which the reflexes are depressed or lost, there are, as a rule, no other signs of involvement of the peripheral nerves. There may be some wasting, which may occasionally be due to a certain degree of malnutrition. It has occurred to Dr. Israel Wechsler and me that to call such a condition neuritis is a mistake; some of my associates and I have thought that the process responsible for these symptoms lies in the spinal cord itself. The demonstration by Dr. Alderman shows that, in this case at least—and I think one is justified in assuming that a similar condition is not infrequent in other cases—the pathologic process is one which affects the anterior horn cells. It may be also that in cases in which the symptoms are more characteristic of neuritis the process is likewise in the cord, and not in the peripheral nerves. Similarly, the idea has been broached that in cases of lead palsy and lead neuritis, and even of alcoholic neuritis, the process is not truly neuritis and should not even be designated as such, because it is not an inflammatory but a degenerative process. Sometimes, it is true, it is difficult for pathologists to differentiate between inflammation and degeneration, but in an instance of this kind in which one finds no evidence of inflammation, such as edema, cellular infiltration and reactive changes in the blood vessels, one is justified in dispensing with the term "neuritis" and in speaking of the condition as neuronopathy or, as Dr. Alderman mentioned, myelopathy.

It is difficult to say what factor causes this condition. It may be a toxin, as Dr. Alderman said. A similar process occurs in pernicious anemia, in which subacute combined sclerosis is unquestionably due to some toxic product associated with the disease. If it is asked why the anterior horn cells alone are involved in the case of diabetes, I ask why in pernicious anemia the anterior horn cells are usually not involved but the posterior and sometimes the lateral columns are the seat of a degenerative process. One cannot answer that question. One knows only the facts. It might be said that in one instance the cell, and in another the tracts, are less resistant to the supposed toxin, but if one tries to answer the question why there is this lack of resistance, one cannot, for want of knowledge.

Dr. Levin demonstrated a histopathologic picture which is, so to speak, a unique presentation by Dr. Globus. I think I am correct in stating that the term "transitional glioma" is Dr. Globus' contribution to the pathologic histology of tumors of the nervous system. In his study of tumors he has come to this differentiation. I believe he is correct in picking out this group of cases of glioma from the large group. I wish he would tell of one or two cases of which I have knowledge, in which he made the diagnosis of transitional glioma from the material given him at operation. When he makes this diagnosis, one recognizes that the glioma is essentially malignant and that he means that it will continue to grow and will recur and eventually cause death. In the instances in which he made this diagnosis there was recurrence of the tumor; in one case there were, I think, three operations, and in another, two. If I am not mistaken—Dr. Globus can verify this—his final diagnosis in one case was spongioblastoma. In other words, this bore out to a certain extent his contention that the diagnosis of the histologic nature of a glioma depends, in some instances at least, on the stage at which the tumor reaches the pathologist. In the cases I have mentioned, the diagnosis of transitional glioma was made at first because the tumor presented the characteristics which Dr. Levin has described; finally, when autopsy or biopsy was performed in the last stage, it showed the characteristics which are designated as those of spongioblastoma multiforme.

Dr. Joseph H. Globus: With regard to the case of diabetic neuronopathy described by Dr. Alderman: There is nothing more to be said about the pathologic changes; I am in full agreement with the interpretation of the pathologic condition as a degenerative process affecting the lower motor neuron, from the cell body

in the anterior horn of the gray matter of the spinal cord throughout the length of the neuron, until it reaches the muscle. The process was characterized by the accumulation of large quantities of fat in the cell body, as well as in the axis-cylinder. However, I am not ready to agree with the concept presented as to the probable etiologic factor. I cannot conceive of a circulating toxin, no matter how produced, affecting a selected part of the nervous system in such an asymmetrical fashion. I am more inclined to believe that the disease is due not to something that has been introduced but to something of which the cell has been deprived and that because of this deprivation the cell has undergone gradual dissolution, leading to death of the neuron.

With regard to the second presentation: I have been so generously quoted that it would be better for me to say no more; however, I wish to answer some of the questions asked. First, what is the importance of recognizing this type of tumor? It is more than an academic problem. Frequently, material obtained by a surgeon in partial removal of a tumor is submitted, and an opinion is requested as to whether it is malignant or benign. The surgeon is inclined to be guided by the answer to this question. If he can be told outright that the tumor is malignant, he knows that further surgical procedures are undesirable. If he can be told that it is benign, he will be tempted to go ahead at the next opportune moment. However, there are tumors which fall between the benign and the malignant, and the inexperienced pathologist may consider them as benign and so entice the surgeon to go ahead, without there being any promise of immediate or lasting results. The patient is subjected to an operation which holds no promise of recovery. If the surgeon can be told that the tumor belongs to the intermediate group and that it is potentially malignant, he can map out his course accordingly. That is the practical side of the problem.

DR. D. ALDERSBERG: I am familiar with the case described by Dr. Alderman, with the permission of Dr. Globus, and I wish to discuss it from a medical rather than from a neurologic standpoint. The frequency of neuropathies in diabetic patients is noteworthy. One sees absence or depression of reflexes and conditions of the peripheral nerves which are frequently called peripheral neuritis, but comparatively rarely changes in the gray matter of the central nervous system; so the case described by Dr. Alderman has a special interest for every one who is interested in this field.

The neuropathies are frequent among incorrectly treated or untreated diabetic patients. There is apparently some relationship between disturbed metabolism and changes in the nervous system in these patients. For many years the explanation has been that some toxic influence caused by diabetes per se or by complications of diabetes or arteriosclerotic changes were responsible, but recent work, such as that of Jordan, of Boston, seems to show that these agents are perhaps not as important as one formerly believed. The whole question is now under revision, and as Dr. Globus pointed out, it is believed that a deficiency manifestation, a deficiency disease, causes the neuropathies associated with diabetes. The disturbance seems to be an avitaminosis and may be compared with alcoholic neuritis.

As far as I know the literature, two facts form the basis and justification for this conception. First, there is a certain similarity between typical avitaminosis (beriberi) and diabetic neuritis. It is interesting that some chemical changes in the nervous tissue in cases of diabetic neuritis, such as a diminished amount of cerebrosides and cholesterol, may be observed in experimental beriberi. The second fact is seen in the results of treatment for diabetic neuropathies with modern vitamin preparations. One of these preparations is crystalline vitamin B_1. Every one who has an opportunity to treat diabetic patients knows that treatment for the diabetic neuropathy has always been unsatisfactory. Even when the diabetes was under adequate control, with normal urine and sugar content of the blood, months elapsed before the patient found relief, if at all. One is favorably impressed with the results of vitamin treatment for diabetic neuritis. I think that treatment with crystalline vitamin B_1 should be supplemented with preparations of yeast. It is a

whole complex and seems to include something that is better than crystalline vitamin B alone, much as one prefers today to use thyroid substance instead of thyroxin.

How can one explain avitaminosis in diabetes? Is it perhaps due to diminished intake, as in cases of alcoholic neuritis? I do not believe this, for an analysis of a few modern diabetic diets for their vitamin B content revealed that they are not poor in this vitamin. Furthermore, diabetic patients who have neuropathies are often persons who exceed their diets. Second, may avitaminosis be due to decreased absorption of vitamins from the intestinal tract, as is seen in some cases of ulcerative colitis? This point apparently has no importance. I know of no facts suggesting impairment of absorption in the cases of diabetic neuropathy. In my opinion, a third possibility must be emphasized, namely, impaired storage or utilization of the vitamins in the body. Clinically experience suggests a relationship between untreated diabetes and diabetic neuropathies. Diabetic patients frequently have enlargement of the liver, caused mainly by various degrees of infiltration of the cells with fat. Fat-infiltrated liver cells show remarkable changes in function. The ability to store glycogen is impaired. A working hypothesis is that in cases of diabetic avitaminosis the changes in the liver may be the cause of impairment in either the storage or the utilization of the vitamin B complex or in both. I believe that the same factor may also be of partial importance in cases of alcoholic neuritis, because enlargement of the liver and infiltration of the liver cells with fat are frequent in cases of chronic alcoholism.

However, nothing is known of the ways in which the vitamin B complex acts on nerve cells. This vitamin seems to promote or to act as a catalyst in oxidation in nerve tissue; but the how and the where are important questions for future research.

EXPOSURE AND DEFENSES OF THE BRAIN OF THE NORMAL NEW-BORN INFANT TO TRAUMA. DR. ABRAM BLAU (by invitation).

Neuropsychiatric sequelae of trauma to the head are relatively infrequent in children. It is noteworthy, too, that sequelae of cerebral birth trauma are not more common in view of the fact that every person is exposed to some degree of cerebral injury at birth. Evidence for this is the normal molding of the head, the high incidence of postnatal subarachnoid hemorrhage and the normal occurrence of fat-containing scavenger glia cells and multiple petechial hemorrhages in the brains of new-born infants. The curious practice of artificial cranial deformation initiated on new-born infants by primitive peoples in various parts of the world also indicates the power of adaptation of the young brain to distorting influences. It thus seems that the young human brain has some capacity to sustain safely a degree of cerebral injury which is impossible for the adult brain. My purpose in this communication is to correlate some well established facts in order to explain the remarkable resistance of the young brain to trauma.

The crucial obstetric problem in man consists of the delivery of the large, round head through the less spacious, fixed curve pelvic passage. In other animals the pelvic canal is simple and the head relatively small; the delivery of the chest and rump is difficult (Stoss). Theoretically, one may presume that the head will be of the smallest possible size to facilitate birth. Some confirmation of this is indicated in the fact that the human fetal head is essentially a brain case and that little of the face is represented, as in other animals. The relevant question is: What is the basis of the large brain at birth?

The minimum constitution of any organ at birth embodies sufficient substance to serve immediate vital needs and adequate potentialities for future developmental purposes. The brain at birth is a remarkable replica of the adult brain, both in size and in form. The body, kidney, liver and heart of the adult are, respectively, 21.3, 13.1, 12.8 and 12.7 times as large as those of the new-born infant; the brain multiplies its weight only 3.7 times (Vierordt). At birth the weight of the brain in proportion to that of the body is 12.3 per cent, while in the adult it is only 2.2 per cent. Even gross structures which have little immediate function and

which contribute greatly to its bulk are fully represented in the new-born brain. The functionless cortex is an example of such structures. The obvious conclusion from these facts is that the brain has little potentiality for growth after birth.

This advanced development of the brain at birth is attributable to the early special differentiation of the essential cells. Maximow stated that as soon as the nerve cells reach an early stage of differentiation, when they can be recognized as neuroblasts, they appear to lose the power of further multiplication. At about the fifth month of fetal life the primitive cortex is already well formed. In mammals differentiation of indifferent cells into neuroblasts appears to cease at or near the time of birth. From this time, the number of nerve elements in the body does not increase. Dedifferentiation and subsequent proliferation do not occur. Accordingly, if any neurons are destroyed by accident or disease, they are not replaced. At birth the brain must be provided with a complete quota of nerve cells for the full life's needs, with additional reserves in case of incidental losses. Growth, in the sense of proliferation of neurons, does not occur in the brain after birth. The subsequent relatively small increase of the brain is due not to the multiplication of nerve cells but to the growth of glial, connective, vascular and other tissues, which are less specialized and are capable of postnatal multiplication.

Man's brain is the largest in the phylogenetic scale in relation to body weight. Its globoid shape before and after birth is also an expression of its comparatively high development. In comparative studies, Ariëns Kappers observed that the brain is more brachycephalic (or less dolichocephalic) and increases in height in proportion to the cephalization coefficients. He accounted for the globoid form as that which affords the greatest content for the smallest surface. The human brain is large and globoid at birth because it is fully endowed at this time with sufficient nerve elements for its development.

The large, round fetal head normally undergoes marked changes in contour which make possible the delivery of the child. The fetal cranium consists of separate, soft bones, held together by the adherent dura mater. The head is molded by the forces of labor. The molding may result in slight diminution of the cranial volume, which causes fluid contents (blood and cerebrospinal fluid) to be expressed. The most important change for delivery, however, consists in alteration of the shape of the head from a globoid to an oval contour. The advantage of this temporary dolichocephalic head is that it presents lesser diameters for delivery, with relatively little sacrifice of the volume of the brain case.

The fetal brain must be pliable in order that it may respond readily to the external molding process by a similar change in shape. This is possible by virtue of a well known property of semifluidity, which has hitherto not received due consideration. The young brain is soft and nearly fluid in consistency, in contrast to the more solid adult organ. Cattell made special note of this softness, and analyses by Kutanin indicated a relatively great water content of the young brain. The soft consistency also serves as a physical safeguard for the valuable allotment of sensitive nerve cells. According to elementary principles of physics, it follows that localized forces directed against the soft fetal brain are disseminated and result in change of shape rather than compression at one point. Such compressive forces might otherwise traumatize the adjacent cells. In the semifluid young brain it is as if the cells were suspended in a free medium, and the forces tend to cause a moderate change of position of the cell with relative impunity of the cell body.

Despite the protective influence of the fluid medium, some nerve cells may nevertheless suffer injury under the conditions of molding and delivery. In addition to these direct forces, circulatory disturbances and petechial hemorrhages endanger many elements. Furthermore, the intercellular connections or neuronic processes (axons and dendrites) are undoubtedly exposed in a fluid medium to greater stresses than the cell bodies. One must therefore look for additional compensatory provisions in the young brain.

The further reparative possibilities are derived from the functional immaturity of the new-born brain. Even though an injured nerve cell body may die, it is possible that an uninjured nerve cell body is capable of some degree of repair

of the processes. More important is the fact that nearly all interrelated neurons have functional connections also with several widely separated regions; when some of these relationships are lost, processes of other cells are capable of assuming the function. The brain can also compensate for some destruction of the nerve cells. The nerve tissue is so constructed that many neurons of similar structure and connections are grouped together to form functional "units" or "systems." If some of the neurons are destroyed, the remaining member of a "unit" may continue to perform adequately the function in question. Only if the entire "unit" is destroyed is the function irreparably lost.

Recent researches point to the cortex itself as the site of the developmental delay of its function. The cortex is both the portion of the brain which is most directly exposed to injury at birth and the part which is least essential for immediate extra-uterine life. Histologically, the cortex of the new-born infant is rich in cells. Wertham and Wertham and others noted that many cortical cells disappear in the normal course of development. It seems therefore that the cellular anlage of the fetal brain is more abundant than is actually needed for later biologic purposes. As has been pointed out previously, recovery from trauma to nerve elements cannot be accomplished by regeneration, but only by the functional substitution of associated reserve cells. There is probably also a greater equipotentiality of nerve cells at birth time. It would be exceptional if some cortical nerve cells were not injured at this time. An established functional organization would be even more sensitive to trauma. Thus, postponement of cortical development until after the most perilous period is a logical economy of growth and possibly one reason for the apparent cortical incompetence. After birth, part or all of the available supply of cells may then be enlisted with impunity in the elaboration of final cortical functional systems.

The young brain probably retains the congenital physiologic resistance to injury during the early years of childhood. There are few other provisions against trauma to the head in the infant. Later, the sensitivity to trauma increases proportionately with the complexity of fixed neuronic organization. However, as the child grows and the adult safeguards gradually make their appearance, namely, the active intelligence, the bony skull and the equilibratory and conditioned reflexes, the need for infantile provisions for defense of the brain is lessened.

Without doubt, trauma to the brain at birth and later may produce obvious neuropsychiatric defects. However, these must arise only when complete systems, including the natal cellular reserves, are destroyed. It is therefore important that the obstetrician should appreciate the natural limits of cranial distortion and trauma which are safely possible in the fetus, so that he may institute the necessary prophylactic measures.

Before concluding, I wish to add that I appreciate the scientific weakness of teleologic argument in biology. The present inquiry is deductive, on the basis of phenomenologic facts, rather than a purposive explanation. The normal recovery after exposure to cerebral injury at birth presents the challenge for interpretation before one can attempt any understanding of true neuropsychiatric defects due to injury of this type. Such discussion at least proposes a new point of departure for future investigations on the problem of birth injury.

DISCUSSION

DR. BERNARD SACHS: It seems to me that Dr. Blau has delivered only part of his paper. I had the pleasure of reading what seemed a much more exhaustive paper than he has presented this evening. Some of the good things that paper contained have not been brought out, so that there is no good reason for some of the remarks I wished to make. However, I am in full admiration of his line of thought and the work he has done and is attempting to do. I shall refer to something in the paper which I read. There were two main divisions. In the first part Dr. Blau seems to be concerned that nature provides at the start a much larger brain than is really needed. I should not worry about that, since nature,

on the whole, is much wiser than man can be. After all, even among medical men, one cannot complain of the extravagance of nature in supplying too much brain. The fact that the brain is proportionately much larger at birth than later in life is a fact that all must appreciate.

The second part of the paper concerns what has long been of interest to me and is as promising for further investigation and research as it was years ago. In this part of the paper there was a statement which I have no doubt is correct, but I must confess that the matter had not made the impression on me that it had on Dr. Blau. With due deference to him, I wish to ask pathologists and pathologic anatomists whether they agree that the brain of the infant is in an almost semifluid state, as compared with that of the adult. No doubt it is much more liquid than the adult brain, but whether this semifluidity is the explanation of the greater resistance to trauma is a point that seems to me to be still open to discussion. In lining up all these observations with the important question of trauma at or during birth, the point which should be especially stressed as a reason that the infantile brain suffers less from trauma than an older brain is the tremendous pliability of the skull. This is a factor of the greatest importance. Another factor in regard to trauma, not only during birth but in later years, is the venous hemorrhage, which is extremely frequent and often widespread. It does most of the damage in cases of trauma in early life. I am sorry that so much of the early anatomic change in this condition is forgotten. Most here probably will not remember the cases reported by Sarah McNutt, in which there was diffuse hemorrhage over almost the entire surface of the cortex.

This question of birth trauma is practical and important, and I hope that Dr. Rongy will be able not only to enlighten those present but to take a message to his fellow obstetricians. Neurologists have been trying to deliver this message for many years; they have maintained that the skull of the infant admits of an unusual, but a limited, amount of compression. There is no doubt from the clinical history in cases of injury at birth that the factor of prolonged labor means more than almost anything else. Peterson and I (*J. Nerv. & Ment. Dis.* **17**:295, 1890) showed that the use of instruments in delivery is far less important in this respect than prolonged labor. It was the old doctrine of the obstetrician that one should not interfere with labor so long as the infant's heart continued to beat. There was permitted a prolonged period of labor which could and should have been terminated much earlier. I shall be glad to hear whether the obstetricians' teaching at present differs from that of former days. After all, it is the long, protracted labor, particularly in case of the first-born, that is responsible for damage in later life. Many years ago I stated that "many children would escape palsies and idiocy if the labor were properly managed." That is still true, and since this problem is being discussed from every angle, one may ask obstetricians to give this their special consideration. There should be some way of cutting short protracted labor, particularly in primiparas. If that were done, an enormous good would result to the community. I hope, therefore, that this message will be carried away tonight.

Dr. Blau stated that Virchow's encephalitis congenita has been abandoned as a unit. I do not know whether he means as a clinical or as a pathologic unit, but it is well to remember that in 1868 Cotard first recognized the importance of traumatic encephalitis as a factor in the causation of partial atrophy of the brain. In speaking of early pathologicoanatomic conditions and the resistance to trauma, I wish to recall that especially in cases of the early, more acute cerebral palsies of children, it was necessary to look for a factor that is responsible for the frequent hemorrhages in children with infectious and other conditions—a factor that is overlooked. I take pride in the fact that I had at the time to read almost all the works on pathologic anatomy before I found a satisfactory explanation. This factor is the frequent occurrence not of arteriosclerotic changes, as in later life, but of fatty degeneration of the arterial and venous systems. Since the importance of generalized fatty degeneration and the disturbance of fat metabolism, especially

in the familial diseases of childhood, has become known, one should bear in mind the significance of fatty degeneration as it occurs in the vascular system of the young child.

DR. A. J. RONGY: Trauma at childbirth, in the majority of instances, results from improper obstetric management of the patient during labor. Bad obstetric care and the frequent severe trauma to the fetal head are due to the fact that the mechanics of labor is not properly understood or correctly interpreted. One has been taught to interpret the various positions the fetal head assumes in the pelvis as a mechanical necessity—that it is a process by which the shortest diameter of the fetal head accommodates itself to the largest diameter of the pelvis—and therefore the mechanics of labor is conceived of as an algebraic progression of the diameters of the fetal head and the pelvis, when in fact it is only a geometric coordination of the fetal head and the pelvic basin during the entire progress of labor.

It is this fundamental difference in the conception of the mechanism of labor which accounts for much of the incompetent management in cases of malposition and malpresentation. The fetal skull is a sphere attached to the trunk by a flexible shaft, the neck. Any one familiar with the fundamental principles of geometry knows that the diameters of a sphere do not form a basis for calculation of its passage through a snugly fitting cavity but that it is the radii of the sphere which make it either possible or impossible for the proximal hemisphere to pass through the cavity.

The fetal head, for all practical purposes, is a true sphere, and it must be governed by the same mechanical principles that govern the movement of a sphere. The complications that arise during labor in cases of malposition are due to the fact that the head loses the properties governing the motion of a sphere and that any stage of labor is to a large degree controlled by the fetal neck and the distance between the fetal neck and the pubic arch. The most tragic injuries to both mother and child during labor come about in an attempt to deliver a child when it is impossible to engage half of the head at any given point in the pelvic cavity. Whether half of the head can be engaged depends on how closely approximated are the fetal neck and the pubic bones. The farther the fetal neck is removed from the pubic bones the less likelihood there is for a hemisphere of the head to become engaged. Pulling the fetal head with forceps without having it embrace a hemisphere of the head, which has no definite relation to the pubic arch, causes the greatest number of injuries to the fetal head.

When obstetricians, as well as general practitioners, will interpret the mechanism of labor in this manner, I am certain that the tragedies of childbirth will be greatly minimized.

I have lived through two periods of obstetric practice: the period when high forceps and the brutal axis traction forceps were used in cases of difficult labor, and the period when cesarean section became the vogue. I remember well the time when the fetal head was so severely traumatized after difficult labor that it took from two to three weeks before the symptoms of trauma subsided in the newly born infant; in retrospect, I come to the inevitable conclusion that, while in cases of more severe head trauma in childbirth the infant did not survive, those who survived apparently severe injuries to the head fared well and were not handicapped, either mentally or physically.

This shows, as Dr. Blau indicated in his paper, that the brain of the young infant has a capacity to regenerate and resume normal function. Dr. Blau makes an interesting point in connection with the anatomic structure of the fetal brain, that is, its fluidity and the less liability to injury because of it.

During the past two or three weeks, I took occasion to investigate the condition of about 21 children who had received severe trauma to the head because of difficult forceps delivery. These children range in age from 6 to 24 years. I found that their physical and mental development is normal and that their intelligence and educational processes progress normally. In fact, a young man who had a severe and complicated delivery and suffered what at the time appeared

to be a severe injury to the head, which took a number of weeks to subside, graduated in medicine this year at the head of his class, and was a brilliant student throughout the period of his academic and professional education.

In order to evaluate properly the real effects of injury to the fetal head at childbirth, the obstetrician in conjunction with the neurologist would have to make a study of a large series of cases over a reasonable period. The subjects would be divided into three groups: children born normally; children delivered with instruments, with various degrees of cranial trauma, and children delivered by cesarean section, when trauma to the head could not take place. Such a study would clarify the problem and would once for all settle the question whether injury to the fetal head during childbirth has any effect on the physical and mental development of the child.

From a purely clinical and empirical standpoint, I am convinced that trauma to the fetal head during childbirth, in the large majority of cases, does not affect the mental and physical development of the child.

Dr. Abram Blau: I do not feel competent to comment on Dr. Rongy's remarks on the mechanics of labor, but I am glad that he made the point that many of the children who seem to undergo severe injury at birth recover. It has been my impression for some time that the injuries which occur at birth are of three types: mild, moderate and severe. The severe injuries are those one sees at the postmortem table, and one knows a great deal about what goes on in the brain in such cases. The mild injuries are those from which the patient recovers and of which he shows no evidence later in life. These are probably the most numerous. The moderate injuries are probably those which result in neuropsychiatric defects later in life and are labeled birth injuries. I think these are not frequent. My impression is that many neuropsychiatric conditions are labeled birth injuries without any justification.

Another point which I tried to bring out in my paper is that surgeons have noted that children withstand trauma to the head well as compared with adults. The discussers have not remarked on this point, but I think that the thesis has a relation to the resistance of the young child, too.

Early Infantile Phases of Development. Dr. Margaret E. Fries.

The development of character traits, neuroses and functional psychoses has been studied from many angles. Nine years ago I expressed the belief that added insight into this study might be gained by using two, then comparatively new, approaches. I employed the synthesizing, or "going forward," method of approach to follow development. I started with the infant and thereby observed "character in the making." I also studied correlatively, as well as singly, all factors contributing to development of personality. This entailed a comprehensive investigation of congenital, environmental and sociologic factors and physical, mental and emotional development. Special emphasis was placed on the interrelationship of these factors. Reports of the initial phase of this work have already been presented.

Two and one-half years ago, I undertook a new investigation to secure further data on the following three problems: (1) How early can characteristic behavior and attitudes be discerned? (2) How long do these so-called patterns persist? (3) How can they be influenced, and how can unsatisfactory patterns be prevented?

In the second investigation I studied and treated the family during the mother's pregnancy; I hope to continue this, as well as the previous study through the children's adolescence. I have been fortunate in having the cooperation of the New York Infirmary for Women and Children and of specialists in many fields. Tonight, Dr. Kurt Goldstein has generously consented to discuss the significance of the neurologic material.

I not only investigated developmental factors but studied how they could be satisfactorily influenced through medical, educative and psychiatric treatment, which was administered when indicated.

The procedure, including the choice of material observed and new methods of recording data, has already been fully reported. In brief: Prenatally, home

visits and psychiatric interviews supplemented routine obstetric service. Thus, factors in the environment were ascertained and, when necessary, attempts at adjustment were made, so that the child would be born into an environment as favorable as possible. Further insight into the mother's condition was gained by observing her behavior, attitudes and verbalizations during labor and delivery. During the lying-in period, the mother and infant were closely observed. Medical and psychiatric treatment was given when indicated; also, throughout the hospitalization continuous twenty-four hour observations were made when possible, since shorter observations did not indicate the interrelationship between such factors as the amount of sleep, nursing, crying, activity, excretions, pulse and respiration. New charts were devised to record data and to indicate the interrelationship of all the factors observed. After hospitalization the entire family was followed medically and psychiatrically during visits at the home and clinic.

Throughout this investigation the material was summarized at frequent intervals, so that the great mass of collected data should not become unwieldy. On the basis of these findings, predictions were made as to probable future development, with indication of the trends and patterns to be followed and the prophylactic measures needed to obviate probable maladjustments.

During the infant's first ten days of life, important factors could be ascertained. However, only by studying these factors correlatively did I appreciate that at the end of the lying-in period the behavior of new-born infants could be classified, in general, into three major groups: overactive, moderately active and underactive. These comparative groups do not connote pathologic states.

It is now appreciated that the physical effects of the so-called normal delivery are greater than had been considered clinically. Many investigators have studied the cerebrospinal fluid and eyegrounds to determine the frequency of hemorrhages. I did not repeat this work, but I noted that in a few cases there was excessive irritability—in others, excessive lethargy—persisting only for from the first three to seven days, while in some infants no great change occurred. I believe that this diminution of irritability or lethargy may be due to the subsidence of a physical injury, such as a cerebral hemorrhage, which the baby had sustained at birth.

The mothers were anxious about these transitory states of irritability or lethargy, but of course they were even more anxious when any gross organic defect was present. The latter defects often caused in the parents—especially unadjusted persons—marked emotional disturbances. These disturbances affected adversely their behavior and attitude toward the child. In this way, a vicious circle was initiated, which affected the child's entire development.

The mother's emotional state may affect the infant not only directly but indirectly. I found that the mother's prenatal emotional state influenced her physical condition, which in turn affected the nutrition of the fetus. The mothers' emotional problems could be alleviated by different measures, depending on the type and severity of the condition. In certain cases educative measures or superficial psychotherapy was beneficial but in mothers with severe neuroses deeper psychotherapy was necessary.

I wish to emphasize that in administering any form of psychotherapy to pregnant women, the ultmost caution should be exercised, in order not to mobilize excessive anxiety, which might precipitate a miscarriage.

In my investigation of the possible causes of the three general types of behavior —overactive, moderately active and underactive—I tried to find out if the state of maturity at birth (that is, at full term) played any role. In order to ascertain the maturity, I used the following expedients: (1) the mother's calculation of gestation; (2) complete physical examination of the infant; (3) anthropometric measurements; (4) roentgenograms of the carpal bones, and (5) neurologic tests.

Drs. Elizabeth Seech and Sonia Stirt assisted in giving the neurologic tests, which included those for auditory, gustatory, sucking, visual, nasal, tactile, postural and superficial and deep reflexes. The responses to all these tests indicated not only the maturity of the nervous system but the infant's general condition, which in turn influenced the excitability of the nervous system. It is obvious that if one were to rely only on the neurologic tests, without studying carefully the congenital and environmental factors, one might derive an inaccurate picture. This is of

special importance when considering the infant's ability to nurse, which is determined by many factors—the sucking reflex being only one.

Of special interest was the ability to hold the head upright and the type of Moro response—which seemed to run parallel. The accompanying moving pictures illustrate how the Moro response diminishes and is supplanted by the startle reaction as the child grows older.

In general, the more mature infant—ascertained by the aforementioned expedients—was comparatively less active, showed a mild Moro response, was better coordinated and stronger, sucked better, slept more quietly, was less irritable, held the head upright for one or more seconds, placed the entire foot flat on the table when held in the standing position and could more satisfactorily endure deprivations. Thus, the more mature infant had not only physical but psychologic advantages, because he could overcome frustrations more readily and derive gratification more easily.

I have cited general characteristics of the more mature infant, but it is conceivable that variations in behavior may result from different combinations of the aforementioned three factors: the general condition and the excitability and maturity of the nervous system. For example, a bad general condition (excitable nervous system) may be combined with an average, premature or postmature nervous system, or a good general condition (qniet nervous system), with an average, premature or postmature nervous system.

Depending on these many combinations, it is possible, for example, to have at least two types of comparatively underactive infants. It is important, particularly for prognostic and prophylactic purposes, to differentiate between these types. The underactive baby who shows a mild Moro response because of postmaturity is able to overcome frustrations and will probably develop into a well adjusted person. The other type of underactive infant, who also shows a mild Moro response—not because of postmaturity but because of diminished excitability of the nervous system—is less able to overcome frustrations and reacts by withdrawal or passivity. Such an infant's behavior may be the prototype of future dementia praecox. It remains to be seen whether these hypotheses are correct and whether maturity at birth is a contributory factor in future adjustment.

In conclusion, I believe that through this investigation I have demonstrated the following points: 1. Characteristic behavior and attitudes have their causes in congenital, environmental and sociologic factors and in physical, mental and emotional development. With the exclusion of gross pathologic change in any single field, the interrelationship of these factors is more important than any isolated factor.

2. There has been established the value of this new methodology for investigating and recording data, as well as the choice of material to be observed and the standardization of the Moro test.

3. At the end of the first ten days of life, three major so-called behavior patterns can be discerned: overactive, moderately active and underactive, with their gradations and subdivisions.

4. These patterns of the first ten days were found to be present at the end of the first year. The predictability of the persistence of these fundamental patterns constitutes part of the program for future work.

5. These patterns can be influenced when medical, psychiatric and educative treatment is administered to the entire family. Such treatment—prophylactic and therapeutic—is easier and more efficacious when started during the mother's pregnancy.

6. A practical way to institute prophylactic mental hygiene is the addition of a psychiatrically trained case worker and a psychiatrist to the personnels of prenatal clinics, obstetric services and well baby and preschool clinics.

DISCUSSION

DR. KURT GOLDSTEIN: It was a good idea to study the behavior of children during the first days of life, in order to use the findings in making a prognosis

for later development, as well as in preparing a means on this basis by which unfavorable development might be prevented. Special consideration was given to the signs of retarded development, particularly to the parallelism of different formations of the Moro phenomenon and the variations in general behavior at different ages. For such a procedure, it is important to be clear as to the kind of reaction this phenomenon represents.

I had the opportunity to make recent observations in respect to the Moro phenomenon by means of the moving pictures taken by Dr. Fries. These pictures allow one to study the individual Moro reactions singly and to compare the changes in the reaction at different stages of development of the child.

The original description by Moro shows that the reaction consists of two parts, involving essentially opposing movements. Immediately after slapping the bed, stretching of the body, tilting of the head backward, abduction and extension of the arms and extension of the hands and fingers take place. In the second phase the arms are flexed and come together; the hands and fingers flex, and both extremities are brought together in front of the chest. Moro, noticing only the second phase, assumed that he was dealing with a clasping reflex resembling that of the infant ape in grasping the body of its mother. If the total reaction is taken into consideration, one is able to distinguish the two phases mentioned. The first phase, in toto, is similar to a muscle pattern which one associates with decerebrate rigidity. This type of reaction—the tendency to extension and abduction of the limbs—corresponds further to phenomena which are observed in association with defects of the cerebellum and the frontal lobe, which I have described as the "to-turning tendency" of the organism to outerworld stimuli (The Function of the Cerebellum from a Clinical Standpoint, *J. Nerv. & Ment. Dis.* **83**:1 [Jan.] 1936). This trend appears if the regulatory cortical influence on reaction is diminished. Every normal reaction to stimuli begins with turning of the organism toward the source of the stimulation. Normally, however, this is only the first step of the reaction pattern, which is followed by a performance adequate to the particular quality of the stimulus. In persons with a lesion of the frontal lobe this reaction consists only of the first step, which appears to be greatly exaggerated. I have called this an abnormal "to-turning" tendency.

I am inclined to believe that the Moro response is a reaction of the same type, caused by the lack of influence of the cortex, especially of the frontal lobe, in consequence of its immature state at this early stage of life. Such lack of influence of cortical impulses can be concluded from the whole behavior of the baby. This may also be demonstrated by the anatomic signs of immaturity of the higher apparatus (the underdeveloped cortex) and of the pathways between the higher and the lower apparatus. This agrees with the assumption that the decrease and, finally, the disappearance of the reaction are parallel to the development of holding the head erect and of sitting and standing, as Dr. Fries has shown in her moving pictures—phenomena concerning which there is no doubt that they correspond to degrees of maturation of the brain cortex.

In line with this assumption, the Moro reaction may be considered a sign of lack of maturity of the highest centers of the brain cortex. The reaction is normal for a definite age period, but it is a symptom of immaturity, and so far is an abnormal, not a normal, physiologic phenomenon. The development of this response, the increase or decrease in its intensity, or its other attributes can be used as an index for the greater or lesser progress of cortical maturation.

In accord with this assumption, the first phase of the reaction is considered to be the characteristic part, contrary to the interpretation of Moro, who stressed the second phase as the essential part. The assumption by Moro of a clasping phenomenon is vague, in that it is not understandable how a clasping reaction would start with extension of the arms and fingers. Close observation of the pattern in early and late stages of development of the child leads to understanding also of the second phase of the reaction. This phase is to be considered as a movement which brings the organism back to the position habitual for the child at the time the reaction is tested. Because the reaction usually is tested at a time

when this habitual position has a flexion pattern, the second phase represents a flexion movement. Later, when the habitual position loses more and more the preponderance of a flexion position, the second phase of the reaction disappears accordingly, at a time when the first phase—even if not as much developed as in the early stage—shows clearly the character of an extension pattern.

This character becomes clear if one compares the Moro pattern with a reaction to very strong stimuli which appears at a time after the Moro reaction has vanished and which shows especially a flexion pattern. This is the startle pattern, described by Strauss and studied recently by Landis and Hunt (*J. Exper. Psychol.* **18**:505 [Oct.] 1935). I cannot discuss this reaction here. I wish only to stress that it represents a reaction of the mature person. Thus, it is totally different from the Moro reaction not only in the preponderance of flexion movements but in its character of a normal reaction, while the Moro phenomenon is a sign of immaturity. The startle reaction would also be useful in studies measuring signs of maturity in children.

PSYCHOTHERAPY IN PSYCHIATRIC PRACTICE. DR. HENRI FLOURNOY, Geneva, Switzerland (by invitation).

Two cases of paranoia are reported, in both of which there were delusions of persecution. The first case was that of a slightly feebleminded boy aged 16, who had lived with an older sister, a daughter of his father's first marriage, from the age of 9 years, when his father died. His own mother had disappeared, and nothing had been heard from her. The sister, who showed a chronic paranoid condition, influenced the boy to the extent that he believed whatever she told him; at the time when he was seen, he imagined that people were trying to kill him and his sister by witchcraft or black magic. He did not dare go out on the street because he imagined that he was followed by a gang and that a certain man wanted to do away with him. The boy was taken from his sister and placed in a boarding-school. The simplest form of psychotherapy sufficed to bring him back to normal life. In ten months he gave up all delusions and fears. The simplicity of the treatment was due to the fact that the mental condition was produced by external psychologic factors. The disturbance was *folie imposée*, a special type of folie à deux.

This case may be compared with one of paranoid delusions of persecution in a woman aged 66. The patient imagined that she was constantly pursued by spies and that the arch-conspirator was a young surgeon of Geneva, whom she often consulted because of varicose veins in the legs. She had numerous delusions of a somatopsychic nature. She also imagined that her son's wife had strange sensations in her body when the surgeon was near, that she must be the surgeon's mistress and that the surgeon persecuted the patient because she was aware of it. The condition in this case is described fully in accordance with the freudian mechanisms of projection, and treatment followed the psychoanalytic principles laid down by Freud. This patient has also fully recovered and has been free from all symptoms for twelve years. She is now 78.

DISCUSSION

DR. LELAND E. HINSIE: It was a pleasure to listen to Dr. Flournoy's communication. His general attitude is obviously practical. Practicability was observed throughout his communication, including the opening remark, which had to do with concrete clinical material. The same fundamental question occurred to Dr. Flournoy that has occurred to many others, namely: What were the factors responsible for the improvement in the clinical condition of the patients? Perhaps, as Dr. Flournoy indicated, one of the factors had to do with the psychoanalytic insight that he was able to give the patients.

The presentation would have had added value if Dr. Flournoy had been able to indicate with some degree of reasonableness what the clinical outcome in his cases might have been had he not employed the special technic that he did. Does

he have any impression as to what might have happened to the patients had they not received any formal therapy? I have the impression which is not sufficiently supported by an extensive number of cases, that some patients exhibit periodic paranoid syndromes. Perhaps Dr. Flournoy was treating such patients. Furthermore, it is possible that the nature of the clinical syndrome was of importance in the outcome. It is my opinion also that when a paranoid syndrome occurs in an adult who has previously exhibited good personal and social integration and who has built his paranoid syndrome around members of the opposite sex, the syndrome may be of periodic character. One of the features that are lacking is comprehensive descriptive psychiatry to form the background and control on the basis of which comparisons may be made when a special type of therapy is employed.

A large percentage of patients with a so-called psychogenic syndrome achieve a level of remission or cure irrespective of any therapeutic attitude taken toward them. I do not mean to imply that psychoanalysis was not instrumental in the improvement of the patients. I can wish only that other important data might be available, so that the evidence would be more convincing.

DR. SMITH ELY JELLIFFE: In some of the vaudeville houses that I attended occasionally in my youth, it used to be a familiar device to have as the last speaker a prestidigitator. He could manipulate from ten to twenty balls in the air, at times interspersed with plates and perhaps other odds and ends. The scheme was to prevent the audience from filing out too abruptly toward the end of the program. I do not hope to be able to hold this group by any such device. I should like to throw up, prestidigitator-wise, for consideration, if possible, some of the numerous psychotherapeutic devices that have been utilized since history has been written. Perhaps I can throw up one ball as a commencement. It will be remembered how they treated Nebuchadrezzar. They turned him out to grass. There are hundreds of hoboes, of psychopaths, in all the countries of the world who are turned out to grass. They get along well in a rough life with the Nebuchadrezzar type of therapy. This, however, is far from the more serious aspects that are demanded of the psychiatrist. What for instance, can we, as psychiatrists do with psychotic patients in our private offices? For the most part, they are sent to institutions. One can do little under the circumstances of private practice, except in rare instances, with certain types of patients, such as those that Professor Flournoy has mentioned. I feel that frequently when, prestidigitator-wise, one tries to treat certain kinds of patients who come into one's office, one may often "drop a plate" and that there may be serious consequences. I refer to certain types of depression. Such patients have always to be scrutinized with a great deal of care by a physician who would try to treat them in his office with any form of psychotherapy. Here one should bear especially in mind the criteria that Kraepelin has laid down. When there are increased agitation, insomnia, depression, slowness of thought and loss in weight, one has to be careful about the suicide problem. Moreover, these patients should not be approached psychoanalytically without considerable caution, and only for diagnosis. As most know, the symptoms such depressive patients express are defenses against their own hidden aggressive impulses; one must build up, not reduce, the defenses of the ego by the technical analytic procedure.

In institutions one can be much more catholic, especially in private institutions such as those in which Professor Flournoy practices. In institutions, psychotherapy can be practiced to its most minute and clinically extreme degrees. Here, psychoanalysis *lege artis* can be carried out. My belief is that the best causal therapy for all types of psychoneurotic disturbances is the psychoanalytic method. This does not mean that all should be treated psychoanalytically. Many psychotic patients are not amenable to analytic therapy, even in private institutions.

Finally, what of the half million persons in the institutions of the United States? Every time I go into such an institution, whether it be for five minutes, a half-hour or a day or two, I come away sad and miserably depressed. I see countless

numbers of persons there, sitting around more or less like dead logs. But this is not the real picture, after all. I know that a great deal is being done. Much enlightened psychotherapy in the form of occupational therapy and therapeutic baths is being carried on. A great deal of careful work has been done. The figures cited by Dr. Hinsie show that at least 40 per cent of psychotic patients recover independently of the specific form of psychotherapy used. Other figures are much more encouraging; this makes one hopeful for the future of psychotherapy for the psychoses in the numerous institutions of this country.

DR. A. A. BRILL: I am indebted to Dr. Flournoy for this interesting and instructive presentation. He presented a method of approach which, far from being simple, is, I believe, important. He showed how certain conditions, like folie à deux, can be influenced in a simple way by suggestion, but when it comes to actual psychoses, such as paranoia, in which the whole personality is involved, one must apply the psychologic principles of Professor Freud.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, Feb. 18, 1937

DOUGLAS A. THOM, M.D., *Presiding*

MENTALITY OF INFANTS RELIEVED FROM HYDROCEPHALUS BY COAGULATION OF THE CHOROID PLEXUSES. DR. TRACY J. PUTNAM.

This report is based on a study of 25 infants with hydrocephalus subjected to the operation of endoscopic coagulation of the choroid plexuses. Forty-seven operations were performed, as the procedure was carried out in two or more sessions in most cases. There were 10 deaths in the hospital after operation, an operative mortality of 22 per cent. This includes, however, those during the developmental period of the operation. There have been only 2 "operative" deaths as a result of the last 14 operations on 10 patients. In all cases there was some diminution in intracranial pressure.

The patients may profitably be subdivided into groups. One is made up of infants with hydrocephalus, apparently of congenital origin, who obviously were mentally defective before operation. They make up the majority subjected to the experimental phase of the operation and account for most of the mortality. Of the 14 patients in this group only 1 survives, and he is almost certainly doomed, although there appears to be relief from pressure a year and a half after operation. Autopsy, performed in 6 cases in this group, revealed cerebral defects incompatible with life.

Another group is composed of infants in whom the hydrocpehalus was the result not of a congenital abnormality but of meningitis. Of the 3 infants in this group, 2 were born prematurely. All were mentally defective before operation. Destruction of the choroid plexus within reach failed to reduce the intracranial pressure to normal limits, and all 3 children have died.

In 2 cases operation was performed not because of enlargement of the head but because of leakage from a sessile meningocele. In both instances operation was delayed until ulceration of the meningocele had occurred, and death resulted from meningitis after a unilateral procedure. In spite of this lack of success, there appears reason to believe that the condition offers a promising field for the operation if undertaken early enough.

This report is concerned chiefly, however, with the late results in a group of 6 patients whose mentality has appeared approximately normal before and after operation. There were no operative deaths in this group. Two children have died: One died in another city, of unknown cause but not of increased intracranial

pressure; the other patient was brought to the hospital with return of increased pressure after a unilateral operation and died of a hemorrhage following ventricular puncture before operation could be carried out on the other side. The patient meanwhile had developed normally except for weakness of one arm.

In a third patient, the head has continued to grow larger, and mental development has been arrested in spite of five operative attempts to relieve pressure. In this instance three circumstances were unfavorable. The operations were performed early in the series, while the procedure was still in an evolutive stage, and there was profuse hemorrhage. The head was the largest in the series before operation. Finally, the child was over 1 year old when operation was first attempted, which makes intervention more dangerous and less effective.

The remaining 3 children have received relief and apparently have developed normally. One is in an institution on account of flaccid paralysis of one leg, which followed repair of a meningocele. The child's mental development is reported to be normal, and the hydrocephalus has been relieved.

The second child, D. S., was seen at the age of 26 months, a year and a half after operation. At that time his head measured 53 cm. He had a fair vocabulary, but could not form sentences. He was able to walk and run, feed himself with a spoon, obey simple commands and recognize objects in pictures. Thus, he easily came up to the standards of the Kuhlmann scale for 2 years in the tests given.

The third, G. H., was operated on at the age of 8 weeks. The head had been growing at the rate of 2 cm. per week, and the intracranial pressure was 320 mm. of fluid under basal conditions. A month after the first operation a relapse occurred, and coagulation was performed on the other side. The patient has been seen at intervals, most recently at the age of 18 months. She was alert and lively. The head measured 55 cm. She was able to walk, say "Mama," "Daddy," "book" and "dog," feed herself with a spoon, recognize the picture of a dog, imitate a gesture, spit unwelcome objects out of her mouth, sing a crude tune and beat time with her hands. Thus, she conforms to all the Kuhlmann tests for 18 months and to some of those for 2 years.

It appears justifiable to conclude that destruction of the choroid plexuses holds some promise of benefit to infants less than 1 year old with hydrocephalus of the developmental type (for example, following operation for meningocele), if they are not obviously retarded mentally. Imbecilic hydrocephalic infants will probably die, whether operated on or not.

DISCUSSION

DR. BRONSON CROTHERS: As a pediatrician, I am glad that Dr. Putnam is willing to intervene in many cases of this type. The usual statistical evidence is, of course, discouraging. The evidence that intellectual progress is adequate after operation is not yet at hand, but all pediatricians welcome a logical, daring attack.

DR. GILBERT HORRAX: I can add little to the discussion. I feel as Dr. Crothers does, and wish to pay my tribute to Dr. Putnam. I have attempted to attack hydrocephalus by the open method, without much success, but, like others, have had operation forced on me in three or four cases. Only 1 child has survived the open method, but it is too early to tell about normal mentality. I have followed the other method, namely, turning back a bone flap with incision through the cortex, because I was not familiar with Dr. Putnam's apparatus. Comparisons are hardly fair. Dr. Crothers has presented the matter as well as any one could, and I agree.

DR. TRACY PUTNAM: I believe that any one who saw one of the group of children who have survived this operation in an acute emergency—say, meningococcic meningitis—would not hesitate to apply life-saving measures. The children appear to be normal mentally now—a small proportion of persons who have grown up with hydrocephalus have normal mentality—and I see no particular reason for fearing their future. That this operation may be a life-saving measure is clearly indicated by the case of the child, apparently normal, who was temporarily relieved by coagulation of one plexus but who died at another hospital of increased intra-

cranial pressure while plans were being made to operate on the other plexus. On the other hand, a certain number of babies will deteriorate but will not die if they are not operated on. I do not see that it can be said that the operation itself is dangerous. It is certainly less dangerous to mind or life than doing nothing.

INTELLIGENCE AND SOCIALIZATION. F. LYMAN WELLS.

This paper appeared in full in the May 1937 issue of the *American Journal of Psychiatry*, page 1265.

Regular Meeting, March 18, 1937

DOUGLAS A. THOM, M.D., *Presiding*

THE VASCULAR PATTERN IN VARIOUS LESIONS OF THE HUMAN CENTRAL NERVOUS SYSTEM: STUDIES WITH THE BENZIDINE STAIN. DRS. A. COLIN P. CAMPBELL, LEO ALEXANDER and TRACY J. PUTNAM.

This article will appear in a later issue of the ARCHIVES.

HYPOGLYCEMIC SHOCK IN THE TREATMENT OF PSYCHOSES. DR. M. SAKEL, Vienna, Austria.

This article was published elsewhere (New Treatment of Schizophrenia, *Am. J. Psychiat.* **93**:829 [Jan.] 1937).

Regular Meeting, April 15, 1937

DOUGLAS A. THOM, M.D., *Presiding*

IMAGERY AND ITS RELATION TO SCHIZOPHRENIC SYMPTOMS. DR. LOUIS COHEN (by invitation).

This article will be published in the *Journal of Mental Science.*

ELECTRO-ENCEPHALOGRAMS IN SCHIZOPHRENIA. DR. HUDSON HOAGLAND, Worcester, Mass.

Electro-encephalograms taken on 6 schizophrenic patients during 35 insulin treatments were studied in collaboration with Dr. D. Ewen Cameron, of the research service of the Worcester State Hospital, and Dr. Morton A. Rubin, of Clark University. After large doses of insulin, the frequencies of the alpha brain waves (Berger rhythms) usually showed a progressive decline of from about 30 to 40 per cent, which paralleled by a time lag of from one half to three quarters of an hour the declining blood sugar curves. A solution of dextrose injected during coma restored the frequency, with a lag along a smooth curve. Our data, with other evidence, are in accordance with the view that alpha frequencies, under the standard conditions present in our experiments, other things being equal, are directly proportional to the rate of carbohydrate metabolism of the cortical cells producing the rhythm.

A new measure of variability of the electro-encephalogram, expressed in centimeters, called the "delta index," is a function of the excess voltage developed for brain waves longer than alpha waves. During insulin treatments the curve for the delta index has a relation roughly inverse to that for the blood sugar. Changes in the electro-encephalogram have been found of value in estimating the progress

of insulinization at the time of treatment. Data are presented showing the hour to hour stability in the delta index for patients without treatment, for comparison with changes in the index during treatment.

In 30 of 35 insulin experiments the delta index after the administration of sugar was less than that before insulin treatment. In about the same proportion of cases there was at least transient improvement after treatment.

The mean delta index for 37 normal persons was 2.1 cm., with extremes of 0.5 and 11 cm. In 34 subjects the index was 3.2 cm. or less, the three highest values being 5, 6 and 11 cm. One normal person when awake gave a value of 0.5 cm., and when asleep, 10.9 cm. Twelve alcoholic subjects gave a mean of 2.5 cm., with extremes of 0.5 and 6 cm. Nine manic-depressive patients gave a mean of 2.8 cm., with extremes of 1 and 5.2 cm. Thirty-one untreated schizophrenic patients gave a mean of 6.6 cm., with extremes of 0.5 and 25.2 cm. Twelve of these values were greater than the mean of 6.6 cm. for schizophrenic patients. Despite differences in the mean values (2.1 for normal subjects and 6.6 for schizophrenic patients), the delta index cannot be regarded in itself as a sign of the schizophrenic state, owing to overlapping of values for the normal subjects and those for patients. The value of the index lies in its relative changes in a given patient.

Eighty-four delta indexes taken on 7 patients showing high pretreatment indexes, each over several weeks of treatment, exhibited, in 88 per cent of instances, complete correspondence with independently determined, fluctuating, objective clinical symptoms. With 2 other patients the indexes corresponded to symptoms in 60 and 70 per cent of instances. These 2 patients were verbally unresponsive and showed little detectable day to day change in symptoms, for correlation with the indexes. In case of patients with "low" pretreatment delta indexes, i. e., 4 cm. or less, who constituted about 50 per cent of a group of 31 schizophrenic patients, analysis by this method could not, of course, be made. In schizophrenic patients we found no brain waves qualitatively different from those in normal persons.

Transient relapses and remissions in a patient who had earlier been released, after apparently successful insulin therapy, correlated completely with specific fluctuations in the delta index.

In 9 instances, with several patients, delta indexes were found to change prior to any objective change in symptoms. Five of these 9 prognostic changes were recorded with one patient. We find the index of value in the treatment with insulin of ambulant patients.

DISCUSSION

DR. FREDERIC GIBBS: My associates and I are using the electrical technic described by Dr. Hoagland in our studies on epilepsy. Recently, we have tried varying the blood sugar level in patients who have a great amount of petit mal activity. Lowering the blood sugar level aggravated the disorder, so that the wave and spike formation sometimes became almost continuous. Raising the blood sugar level abolished this formation in all cases.

That both epilepsy and schizophrenia can be influenced by carbon dioxide has been recognized for some time. Now it appears that both can also be influenced by variations in blood sugar. It is gratifying to find that our data are in general accord with those of Dr. Hoagland. The advances which he has reported should be heartening to all who are interested in brain physiology, particularly to those concerned with the study of schizophrenia.

DR. HALLOWELL DAVIS: Mrs. Davis and I have been carrying on a similar series of studies on psychotic patients at the McLean Hospital. We are grateful to Dr. Hoagland if this measure of slow wave activity gives us an index. We have used it, and our range of normal variations coincides with that observed by Dr. Hoagland. These data can be passed around and notes compared. Increase in slow wave activity indicates physiologic depression of cortical activity. This increase also appears in conditions of impaired consciousness, such as fainting due to cortical anemia. Walter (*Lancet* **2**:305 [Aug. 8] 1936) recently reported from

London that in the neighborhood of a cortical tumor there are waves of this type, not from normal tissue or from the tumor but from the boundary zone. Slow wave activity appears to be a delicate and very useful indicator of the state of the cortex.

DR. HERBERT H. JASPER: Dr. P. Solomon and I have recently finished electro-encephalographic studies on a group of 63 schizophrenic patients at the State Hospital for Mental Diseases, Howard, R. I. Our results are in accord with the early reports of Berger on schizophrenia; that is, the records fall within normal limits. Lemere also obtained records within normal limits on schizophrenic patients studied at the National Hospital, Queen Square, London. Travis and Malamud (*Am. J. Psychiat.* **93**:929, 1937) reported records within normal limits in 8 cases in the Iowa State Psychopathic Hospital. In the records for our 63 patients, we have been unable to see anything clearly unlike that sometimes obtained with normal subjects. Perhaps Dr. Hoagland can explain why his results differ from those of the majority of investigators. The slow waves observed by Dr. Hoagland have been found in some pathologic conditions, but not in schizophrenia. The only finding that we might consider at all characteristic of schizophrenia is a rhythm the opposite of slow waves, namely, rapid potentials of low amplitude, with little alpha rhythm. A record of this type is, however, characteristic of some normal persons and may be produced in normal subjects with emotional tension. Slow waves seem to be associated with depression of cortical function, and fast waves, with excitation; our results therefore indicate a tendency to a condition the opposite of that observed by Dr. Hoagland. The last paper of Berger was of interest in this connection; he observed slow waves during insulin coma. He found a close similarity between these records and those taken during other kinds of coma and in cases of poisoning with illuminating gas. His records again showed activity within the normal range for schizophrenic patients. The weight of evidence, so far as the number of cases is concerned, is not in accord with the findings of Dr. Hoagland. Can the difference be due to the selection of cases or to differences in technic?

DR. D. EWEN CAMERON: One of the major questions is: If electro-encephalography constitutes a measure, what actually does it measure? Whether it measures the tension of the individual patient is not apparent at present. We have that also in mind.

DR. HUDSON HOAGLAND: In reply to Dr. Jasper, I wish to emphasize that it has not been possible to separate persons into normal and schizophrenic groups on the basis of differences in the electro-encephalograms. A single record for an individual person is not diagnostic, despite the fact that the delta index for our schizophrenic group averages about 4 cm. above that for our normal group. From the protocols reported, it is clear that there is a considerable overlap in index values. Unless indexes are actually measured, and other workers have not measured them, comparisons are not significant, since to the eye, unpracticed in these measurements, differences of the order of 2 or 3 cm. are often qualitatively indistinguishable in the appearance of the tape. It is not surprising that the small difference in means between our groups should fail to be noticed by qualitative methods of analysis. A still more probable reason that others have not noted the significance of long waves in schizophrenic subjects is that, as far as I know, there are no other studies involving the following of the individual patient whose psychosis is shifting over long periods. We should not have noticed the significance of the slow waves if they had not been modified by insulin treatment. It is the relative day to day change in the index of the individual patient that is of interest, not the mere statistical comparison of groups of persons. This is fortunate, since one wishes to know the progress of a given patient rather than group differences. For the individual patients with pretreatment indexes greater than 5 cm., about 50 per cent of our group of 31 schizophrenic patients, the daily shifts in the index were helpful (see the article by Cameron, Rubin and me [*Am. J. Psychiat.* **94**:183, 1937] for a full discussion of the delta index as a clinical aid, with oscillographic

reproductions showing characteristic marked variations in the long wave potentials with progress of the psychosis).

Some selection of patients may have been operative. This applies especially to the patients in our series who were receiving insulin, since we endeavored to select those in whom the disease had developed recently and to avoid those who were reconciled to an institutional environment. We have observed that patients of the latter class tend to have low indexes. Persons with low initial indexes are obviously unsuited to analysis of this type. Different institutions may also exert selective action with respect to schizophrenic types.

Elsewhere, Rubin and Cameron and I (*Am. J. Physiol.* **120**:559, 1937) have shown that differences in the speed of tape, amplification, time constant and size of electrodes markedly affect the measurement of the delta index. These determinants vary in different laboratories and hence render inappropriate comparisons of delta indexes, even if the indexes have been measured from records taken under nonstandardized conditions. In our clinical paper (*Am. J. Psychiat.* **94**:183, 1937), we showed oscillograms made on several of our patients by visiting workers with an independent amplifier and undulator. These records were obtained under the standard conditions in our experiments and simultaneously with oscillograms taken with our own apparatus from the same pair of electrodes and on the same patients. The two synchronized tapes showed virtually superimposable oscillograms and delta indexes ranging with different patients from 1 to 12 cm. These indexes were identical for the two recording systems within the experimental errors common to either system alone.

It is known that a variety of factors may modify the delta index. It serves, for example, as a sensitive index of normal sleep. It is possible that the index may shift in a number of psychotic and neurotic disorders. This, however, does not militate against its usefulness in relation to the problem of schizophrenia.

OXYGEN METABOLISM IN SCHIZOPHRENIA. DR. R. G. HOSKINS.

This article appeared in full in the December 1937 issue of the ARCHIVES, page 1261.

Regular Meeting, May 20, 1937

DOUGLAS A. THOM, M.D., *Presiding*

THE AUTONOMIC PHARMACOLOGY OF THE EYE, WITH ESPECIAL REFERENCE TO THE ARGYLL ROBERTSON PUPIL. ABRAHAM MYERSON, M.D., and WILLIAM THAU, M.D.

This article will appear in a later issue of the ARCHIVES.

LUMBAR SPINAL FLUID PRESSURE. DR. THEODORE J. C. VON STORCH.

The cerebrospinal fluid envelop consists of the cranium and vertebrae, the membranes enclosed therein and its enclosed and emissary blood vessels. This craniovertebral system is not completely elastic, that is, directly exposed to atmospheric pressure. If it were, it could not support subatmospheric pressures such as exist after certain types of encephalography or after intravenous administration of hypertonic solutions. Nor is it a rigid system. If it were, there would be no further displacement of fluid from it into a lumbar manometer on assumption of the erect position. Therefore the craniovertebral cerebrospinal fluid envelop is semirigid, or semi-elastic—neither a closed nor an open box.

The cranium, vertebral column and ligaments and the portion of the dura applied to bone may be considered rigid. The spinal dura is an inelastic bag capable only of collapse, and the arachnoid applied to it may be considered in the same light. The extradural vascular bed and the intradural vessels with their investing arach-

noid are highly elastic. The mass of nerve tissue may be omitted in a consideration of the sudden changes of pressure due to posture.

Elasticity may be afforded to the system by alterations in volume of the dura or of the vascular bed. Of the latter, the thin-walled arterioles, capillaries and venules are enormously more elastic than the thick-walled arteries and venous sinuses. The venous pressure controlling capillary pressure is probably the most important factor in pressure changes due to posture.

It is to be emphasized at this point that, strictly speaking, observations with the common spinal fluid manometer reflect changes in volume within the ventriculosubarachnoid space. Pressures are only inferred from these volume changes. These alterations of volume are a direct result and measurement of the elasticity of the system.

What is responsible for the lumbar spinal fluid pressure when the subject is recumbent? This pressure is the resultant of the forces for production and for absorption of the cerebrospinal fluid. It is dependent on osmosis, dialysis, selective secretion and intravascular pressure changes, mainly venous. It is well known that transitory increases in arterial pressure cause a parallel change in cerebrospinal fluid pressure. Merritt and Fremont-Smith showed, however, that persistent arterial hypertension does not cause a persistent increase in spinal fluid pressure. In cases of cardiac decompensation with increased venous pressure, the cerebrospinal fluid pressure may or may not be elevated. Loman showed that in various horizontal positions the cerebrospinal fluid pressure varies directly with the venous pressure.

What causes the increase in lumbar spinal fluid pressure when the subject is erect? As the average human being is (or should be) erect two thirds of each day, the question is pertinent to normal intracranial physiology. Weed and Flexner maintained that in the dog, cat, macaque and chimpanzee the lumbar spinal fluid pressure with the animal in the erect position is caused by collapse of the cervical dura, allowing downward displacement of cerebrospinal fluid. Loman and his co-workers observed in man that the lumbar spinal fluid pressure in the erect position is unrelated to that in the recumbent position, is often similar to the calculated lumbar venous pressure and is usually approximately equivalent to the vertical distance from the lumbar puncture needle to the cisterna magna. I have had the good fortune to confirm all Loman's observations in man. However, as the right auricle acts as an outlet between two vascular systems of different resistances, the internal jugular pressure observed by him cannot be used to calculate lumbar venous pressures. Therefore, since I believe that Weed's observations on animals are not strictly applicable to man and that more crucial experiments are necessary to confirm Loman's inferences, I approached the problem from another angle.

Two elastic elements of the craniovertebral system might be responsible for the sudden increase in lumbar pressure in the erect position: venous vascular alterations within the head or the vertebral sac and alterations of the vertebral dura in the nature of collapse or expansion.

Expansion of the vertebral dura is unlikely, in consideration of its inelastic composition. If it did occur, the dura would retain within the vertebrae more fluid in the erect than in the recumbent position and would thus decrease the amount of fluid in the lumbar manometer. Therefore, expansion of the vertebral dura could not be responsible for the increase in lumbar spinal fluid pressure in the erect position. Collapse of the cervical dura will be considered later.

The difference between the spinal fluid pressure in the recumbent and that in the erect position is dependent on the elastic elements of the craniovertebral system. Therefore, alterations in this difference in pressure reflect alterations in the elastic factor. Working on this basis, Dr. E. A. Carmichael, of the National Hospital, Queen Square, London, and Dr. T. E. Banks, of the physics department of St. Bartholomew's Hospital, London, and I were able to determine which elastic factor is responsible for the lumbar spinal fluid pressure when the subject is in the erect position.

We first demonstrated that there is no mathematical relationship between the lumbar spinal fluid pressure in the erect and that in the recumbent position. Neither can be computed from the other. We then demonstrated that there is an approximate similarity between the lumbar spinal fluid pressure in the erect position and the vertical distance from the puncture needle to the cisterna magna. These observations confirm those of Loman.

We then altered the intracranial venous volume and elasticity by graduated jugular compression with the patient recumbent. When this compression was maintained in the erect position, the difference in pressure produced by posture remained the same. Thus, distention of the intracranial veins, though decreasing their elasticity, had no effect on the difference between the spinal fluid pressures in the recumbent and in the erect position. Therefore, alterations in intracranial venous volume and elasticity are secondary to, not productive of, the lumbar spinal fluid pressure in the erect position.

The same results were obtained when the cerebrospinal fluid volume was increased by subarachnoid injection of physiologic solution of sodium chloride. When we repeated these experiments with abdominal instead of jugular compression, we observed that the difference in pressure decreased with increasing distention of the lumbar veins. Thus, by decreasing the potential elasticity of the lumbar veins the difference in pressure is likewise decreased. This suggests that the lumbar spinal fluid pressure in the erect position is a reflection of the lumbar venous pressure.

These observations were substantiated by experiments on patients with complete subarachnoid block due to confirmed subarachnoid tumor. In such patients the normal pressure in the erect position was observed. Thus, neither intracranial vascular changes nor collapse of the vertebral dura acting above the block could be productive of the normal lumbar spinal fluid pressure present below the block when the subject is in the erect position.

The only hydrodynamic structure which passes the block is the anastomotic column of valveless veins. Alterations in their volume would not be affected by the block. The lumbar venous pressure is thus capable of producing normal spinal fluid pressure below a block.

In résumé, it may be said that the normal erect lumbar spinal fluid pressure in man is a reflection of the venous pressure and volume in the lumbar subarachnoid veins. This pressure is dependent on the right auricular cardiac pressure and the vertical distance from the auricle to the puncture needle. The sum of these approximates the lumbocisternal distance, thus explaining the approximate correlation between this distance and the lumbar spinal fluid pressure in the erect positions.

FACTORS RESPONSIBLE FOR THE DEVELOPMENT OF DELUSIONS OF JEALOUSY IN A PATIENT. DR. MORRIS YORSHIS.

The following factors were responsible for the development of delusions of jealousy in this case: (1) status of an adopted child; (2) identification with and jealousy of the mother; affection for the father; (3) early conditioning to the mother's ways, especially to domination of the father; (4) marriage "beneath her" financially and socially, to retain the upper hand; (5) development of interests along lines the mother wanted, with projection of blame on the husband; (6) discord in the marital state leading to revengeful acts, such as illicit sex affairs; (7) relationship of domination and jealousy between the mother and the patient, like that between the patient and the secretaries for whose employment she was responsible, and (8) possible repressed homosexuality (mother and her best friend).

This case, in which the patient followed simple therapeutic suggestions, supports the opinion that patients with such ideational trends can be benefited by psychotherapy.

Book Reviews

Beiträge zur Pathologie des Thalamus opticus. By Paul Schuster. Pp. 324, with 25 illustrations. Berlin: Julius Springer, 1937.

The large size of the optic thalami and their wealth in gray matter, blood vessels and connections with such important structures as the hypothalamus, striated bodies, internal capsule, external geniculate bodies, subcortex and cortex should suggest also a wealth of physiologic and clinical features. The five thalamic blood vessels, which are derived from both the vertebral and the carotid arterial system, supply certain territories, including the gray substance (various nuclei). Involvement of these vessels produces characteristic clinical syndromes, which Schuster has attempted to outline in four contributions (218 pages) (*Arch. f. Psychiat.* **105**:358 and 550, 1936; **106**:13, 1936; **106**:201, 1937), on the basis of clinicopathologic studies in thirty-eight cases. In practically all cases there was softening, which in eight instances could be traced to lesion of a blood vessel. Lesion of the thalamogeniculate artery (which supplies the lateral nucleus of the optic thalamus) was observed to give the typical thalamic syndrome described by Dejerine and Roussy (pain, ataxia and slight disturbances of sensibility), to which Schuster adds a peculiar form of hyperesthesia (hyperpathia; a slight touch with a pin, for instance, causes severe pain) and the so-called thalamic hand (overextension of the terminal and middle joints of some fingers). Lesion of the thalamoperforate artery (which supplies both the medial and the lateral nucleus and the most caudal parts of the optic thalamus, the substantia nigra, the red nucleus and the hypothalamus) causes hemiparesis with hypotonia, ataxia, athetosis and chorea, but no pain and only mild disturbances of sensibility. Lesion of the tuberothalamic artery (which supplies the proximal parts of the optic thalamus up to the nucleus ruber) causes no motor or sensory disturbances, but only a spontaneous feeling of cold, paralysis of lateral gaze and the so-called doll head phenomenon—the patient's eyes roll down when the head is bent. Lesion of the lenticulo-optic artery (which supplies the corpus striatum, the upper part of the optic thalamus and the internal capsule between the optic thalamus and the putamen) causes diminution of sensibility throughout the body and, to some degree, over the face, with marked vasomotor and trophic disturbances. Of sensory manifestations Schuster mentions an anosognosia, which is a motor illusion. Clinically, it was shown as a phantom limb phenomenon; the patient, for instance, believed he actually was performing, on command, movements with the extremities which were paralyzed and thus were unable to move at all. Sometimes the disturbance was combined with hyperpathia and was caused by small foci of softening. Schuster thinks that anosognosia signifies a thalamocortical rather than a thalamic lesion but that it may also be of sympathetic nerve origin.

Lesion of the fifth thalamic, or choroid artery (which supplies among other structures the upper and inner portions of the optic thalamus and the posterior part of the pulvinar) in a few cases caused softening of the caudal portions of the optic thalamus. Clinically, there were disturbances of deep sensibility, hyperpathia, hypertonia and the thalamic hand, but Schuster realizes that some of the clinical manifestations were due to complex or multiple vascular lesions.

Complex vascular lesions of the thalamus are much more common than isolated vascular involvement and are difficult to differentiate from suprathalamic or cortical changes (the thalamocortical fibers). Schuster asserts that the various sensory manifestations, including hyperpathia, as described in thalamic foci, occur also in suprathalamic and cortical lesions, that the cortex and thalamus possess the same "somatotopic structure" and that the sensory cortex and the optic thalamus are in many respects a functional whole. In this connection, Schuster discusses in detail the numerous signs and symptoms (sensory, motor, vasomotor, trophic, psychic and others) that have been described in thalamic lesions. It is remarkable that in five of the thirty-eight cases disturbances of sensibility were absent, regardless of the size of the focus, and that superficial sensibility was

as much and as frequently affected as the deep variety. Superficial sensibility is probably supplied to each half of the body by both thalami, while deep sensibility is supplied by the contralateral optic thalamus. The sense of touch was reduced more often than that of pain, and the sense of pain more often than that of temperature. Hyperpathia with spontaneous pain and feeling of cold was present in eight cases and, as Schuster believes, was due to a lesion of the lateral nucleus of the optic thalamus. The medial nucleus of the optic thalamus hardly possesses a sensory function, for it may be destroyed and cause no disturbances of sensibility provided that the pulvinar is preserved. According to Schuster, the pulvinar is the keeper of sensibility in man, while the thalamus regulates and modifies the afferent sensory stimuli. It is an inhibitory apparatus.

Many other topics are discussed in detail: Hemiplegia and hemiparesis were associated with hypotonia and pathologic reflexes, vasomotor and trophic, but not with sensory disturbances; ataxia was not a constant sign but was probably overshadowed by choreatic and athetotic movements which, like the tremor, are manifestations of a lesion of the extrapyramidal tract. Extrapyramidal lesions, according to Schuster, are also the basis of dissociated paralysis of the facial nerve, in which mimical and not voluntary movements of the face are paralyzed. Among other interesting topics discussed are paralysis of lateral gaze, cataplexy and psychic disturbances, but the majority of these manifestations could not be adequately interpreted, as the patients were old and the disease was of long duration.

The conclusions arrived at by Schuster as to the possible function of various parts of the optic thalamus, problematic as some may appear, deserve great attention, for they are based on facts brought out by careful clinical and pathologic observations.

Agnosia, Apraxia, Aphasia: Their Value in Cerebral Localization. By J. M. Nielsen and J. P. FitzGibbon. Price, $3. Pp. 210, with illustrations. Los Angeles: The Los Angeles Neurological Society, 1936.

This monograph consists of three parts. Part 1 gives a general account of the subject, ably covering the more important phases through which the doctrine of the aphasias has passed since the days of Broca. In part 2 case reports are presented and methods of examination discussed. Part 3 is given over to definitions and general terminology.

The study is based on the authors' personal experience in two hundred and forty cases. Of these, autopsy was performed in twenty-five and the diagnosis was verified at operation in thirteen and corroborated by roentgenography in two. Unfortunately, it is not stated whether the two hundred and forty cases were invariably studied with the same method. From the individual case reports it is apparent that the method of study was not strictly uniform. Comparability thus was not secured. Another defect of the investigation is the absence of serial sections in the cases in which autopsy was performed. Since Dejerine's criticism, it ought to be an established principle that anatomic conclusions from autopsy material with regard to the aphasias must be based on serial sections. In spite of the fact that the authors' studies were limited to global sections, the inferences concerning localization are rather daring. Thus, it is stated, partly on Henschen's authority and partly on the basis apparently of the authors' experience, that "the anterior-superior portion of the angular gyrus was more concerned with verbal agnosia than the posterior portion. From the above we see that the posterior-inferior portion is probably more concerned with revisualization of verbal images" (page 49).

Part 1 is undoubtedly of value to the student of the aphasias. The authors give here in succinct, antithetic diction apt explanations of the terms current in the literature. Exception might be taken to a number of the definitions offered, but the effort to present clearcut definitions deserves credit.

The book is too technical to be recommended to the beginner. But the neuropsychiatrist with even a moderate experience in the field of the aphasias will find his effort amply rewarded if he will take the trouble to peruse carefully the eighty-four pages of part I.

Sitz und Wesen der Krankheiten im Lichte der topistischen Hirnforschung und des Variierens der Tiere. Erster Teil. Befunde der topistischen Hirnforschung als Beitrag zur Lehre von Krankheitssitz. By Cecile Vogt and Oskar Vogt. Pp. 221, with 271 illustrations. Leipzig: Johann Ambrosius Barth, 1937.

This monograph by Cecile and Oskar Vogt presents new evidence in favor of the authors' theory of pathoclisis. It is written in a complicated style, but it is beautifully and profusely illustrated and well printed and represents an excellent bit of research in brain physiology.

The Vogts believe not only that specific cerebral structure is associated with specific functions but that specific areas of the brain are associated with certain types of disease processes, the specificity depending on the structure of the brain and on physicochemical processes (pathoclisis). They speak of a general, a specific and a singular type of pathoclisis. General pathoclisis is illustrated by the greater susceptibility to disease of the precentral gyrus and the putamen as compared with that of the nucleus ruber. Specific pathoclisis is seen in the capacity of a part of the brain to react to different processes in the same way. Thus, the hypermyelination of the striatum as a result of traumatic, infectious and vascular factors represents specific pathoclisis. Singular pathoclisis is a tendency to react to a definite disease by an unusual process. Specific pathoclisis may develop later into the singular type.

This represents the views on pathoclisis in general. There are many other factors in the argument. For example, a specific area of the brain attacked by a disease process may be involved as a whole, in part or in multiple foci. The Vogts regard the susceptibility to disease of Sommer's sector in the cornu ammonis as an example of pathoclisis. They deny that the changes observed therein are due entirely to vasomotor factors. Another example is found in the susceptibility to disease of the putamen and pallidum under all sorts of conditions. The Vogts extend their observations now to assert that many focal diseases of the brain show a topical or predilective character and that this holds not only for hereditary diseases but for those of toxic, infectious and vascular origin.

The monograph is an able exposition of the Vogts' famous theory of pathoclisis and offers the latest contribution of the authors to the theory in question. It should be read by all neuropathologists, neuro-anatomists and neurophysiologists.

The Morphine Habit and Its Painless Treatment. By G. Laughton Scott, M.R.C.S., B.A. (Oxon). Second edition. Price, 5 shillings. Pp. 106. London: H. K. Lewis & Co., Ltd., 1937.

This is a small, nicely written treatise on the treatment for morphine addiction. The type of treatment advocated is the gradual reduction of morphine with the maintenance of constant vagal preponderance through building up a high tolerance for belladonna. As a whole, the book does not seem especially scientific, but it is of value as a straightforward account of clinical experience. Although a number of case records are described, no particular cases are cited as controls. For practitioners who may be interested in the variations of treatment for drug addiction, this would seem to be practical reading.

News and Comment

AMERICAN ORTHOPSYCHIATRIC ASSOCIATION

The Fifteenth Annual Meeting of the American Orthopsychiatric Association will be held at the Stevens Hotel, Chicago, Feb. 24, 25 and 26, 1938. Secretary: Dr. Norvelle C. LaMar, 210 East Sixty-Eighth Street, New York.